> FILE REG

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STRUCTURE FILE UPDATES: 21 JUL 2010 HIGHEST RN 1233453-03-6 DICTIONARY FILE UPDATES: 21 JUL 2010 HIGHEST RN 1233453-03-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

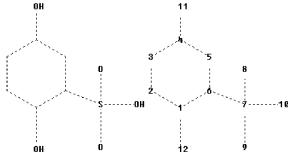
TSCA INFORMATION NOW CURRENT THROUGH January 8, 2010.

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

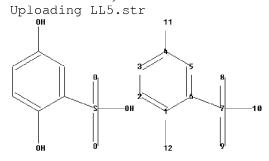




chain nodes : 7 8 9 10 11 12 ring nodes : 1 2 3 4 5 6 chain bonds : 1-12 4-11 6-7 7-8 7-9 7-10 ring bonds : 1-2 1-6 2-3 3-4 4-5 5-6 exact/norm bonds : $1-2 \quad 1-6 \quad 1-12 \quad 2-3 \quad 3-4 \quad 4-5 \quad 4-11 \quad 5-6 \quad 6-7 \quad 7-8 \quad 7-9 \quad 7-10$

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS



chain nodes :
7 8 9 10 11 12
ring nodes :
1 2 3 4 5 6
chain bonds :
1-12 4-11 6-7 7-8 7-9 7-10
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-12 4-11 6-7
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-9 7-10

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS

AUTHOR SEARCH

=> FILE HCAPLUS

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FILE COVERS 1907 - 22 Jul 2010 VOL 153 ISS 4

FILE LAST UPDATED: 21 Jul 2010 (20100721/ED)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2010

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2010

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2010.

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Page 2 of 46

http://www.cas.org/legal/infopolicy.html

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This file contains CAS Registry Numbers for easy and accurate substance identification.
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'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> FILE WPIX

FILE 'WPIX' ENTERED AT 17:21:54 ON 22 JUL 2010 COPYRIGHT (C) 2010 THOMSON REUTERS

FILE LAST UPDATED: 21 JUL 2010 <20100721/UP>
MOST RECENT UPDATE: 201046 <201046/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> Now containing more than 1.6 million chemical structures in DCR <<<

>>> IPC, ECLA, US National Classifications and Japanese F-Terms and FI-Terms have been updated with reclassifications to end of March 2010.

No update date (UP) has been created for the reclassified documents, but they can be identified by specific update codes (see HELP CLA for details) <<<

>>> FOR THE LATEST DERWENT WORLD PATENTS INDEX (DWPI)
STN USER DOCUMENTATION, PLEASE VISIT:
http://www.stn-international.com/stn_dwpi.html <<<

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

>>> For changes in DWPI see HELP CHANGE - last updated April 6, 2010 <<<

>>> New display format ALLSTR available - see NEWS <<<

>>> US National Patent Classification thesaurus added - see NEWS <<<

=> D STAT QUE L52

L41	113	SEA	FILE=WPIX	SPE=ON	ABB=ON	PLU=ON	SANCHEZ P?/AU
L42	21	SEA	FILE=WPIX	SPE=ON	ABB=ON	PLU=ON	GARRIDO A?/AU
L43	13	SEA	FILE=WPIX	SPE=ON	ABB=ON	PLU=ON	GALLEGO G?/AU
L44	142	SEA	FILE=WPIX	SPE=ON	ABB=ON	PLU=ON	LOPEZ S?/AU
L45	8	SEA	FILE=WPIX	SPE=ON	ABB=ON	PLU=ON	PUERTO R?/AU
L48	2	SEA	FILE=WPIX	SPE=ON	ABB=ON	PLU=ON	L41 AND ((L42 OR L43 OR
		L44	OR L45))				
L49	1	SEA	FILE=WPIX	SPE=ON	ABB=ON	PLU=ON	L42 AND ((L43 OR L44 OR
		L45))				
L50	1	SEA	FILE=WPIX	SPE=ON	ABB=ON	PLU=ON	L43 AND ((L44 OR L45))
L52	2	SEA	FILE=WPIX	SPE=ON	ABB=ON	PLU=ON	(L48 OR L49 OR L50)

^{=&}gt; DUP REMOVE L33 L52

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PROCESSING COMPLETED FOR L33 PROCESSING COMPLETED FOR L52

L60 7 DUP REMOVE L33 L52 (0 DUPLICATES REMOVED)

ANSWERS '1-5' FROM FILE HCAPLUS ANSWERS '6-7' FROM FILE WPIX

=> D L60 IBIB ABS HITIND HITSTR 1-5; D L60 IBIB AB HITSTR 6-7

L60 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:331043 HCAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 148:547206

TITLE: Synthesis and structural characteristics of highly

graphitized carbon nanofibers produced from the

catalytic decomposition of ethylene: Influence of the active metal (Co, Ni, Fe) and the zeolite type support

AUTHOR(S): Romero, Amaya; Garrido, Agustin;

Nieto-Marquez, Antonio; Sanchez, Paula; de

Lucas, Antonio; Valverde, Jose Luis

CORPORATE SOURCE: Facultad de Ciencias Quimicas/Escuela Tecnica

Agricola, Universidad de Castilla-La Mancha, Ciudad

Real, 13071, Spain

SOURCE: Microporous and Mesoporous Materials (2008), 110(2-3),

318-329

CODEN: MIMMFJ; ISSN: 1387-1811

PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to study the influence of the metal phase in the carbon yield and structural characteristics of carbon nanofibers (CNFs) synthesized by CVD over supported catalysts, different catalysts were prepared using iron, cobalt and nickel as active metal and zeolites Y and mordenite as support. The results showed that the metal precursor produced a great influence on the catalytic activity, fact that could be explained in according to the different solubility of carbon in the metals or in the differences in the diffusion and segregation of carbon through the metal particles. Characterization data of the solid carbon products revealed unique structures and textural properties as well as crystalline conditions on function of metal used. Addnl., support-metal interaction was evaluated, where expts. with similar nickel load over Y and mordenite zeolites were carried out, finding higher carbon yields and more ordered structures when Y zeolite was used.

CC 67-3 (Catalysis, Reaction Kinetics, and Inorganic Reaction Mechanisms)

Section cross-reference(s): 66, 75

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD

(5 CITINGS)

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2005:1032532 HCAPLUS Full-text

DOCUMENT NUMBER: 143:464206

TITLE: Growth of Carbon Nanofibers from Ni/Y Zeolite Based

Catalysts: Effects of Ni Introduction Method, Reaction

Temperature, and Reaction Gas Composition

AUTHOR(S): de Lucas, Antonio; Garrido, Agustín;

Sanchez, Paula; Romero, Amaya; Valverde, Jose

L.

CORPORATE SOURCE: acultad de Ciencias Quimicas y Escuela Tecnica

Agricola, Departamento de Ingenieria Quimica,

Universidad de Castilla La Mancha, Ciudad Real, 13071,

Spain

SOURCE: Industrial & Engineering Chemistry Research (2005),

44(22), 8225-8236

CODEN: IECRED; ISSN: 0888-5885

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

Results of thorough studies of the catalytic synthesis of carbon nanofibers (CNFs) AB by the decomposition of ethylene using Y zeolite as the support and Ni as the active phase were discussed. Exptl. results clearly indicated that the metal-incorporation method (ion exchange or impregnation) had very significant effects not only on CNFs growth but also on the deactivation rate, the final yield of CNFs, and the characteristics of the synthesized CNFs. CNFs synthesized from the impregnated catalyst grew from small and well-dispersed Ni particles anchored to the outer surface of the zeolite. Nevertheless, CNFs synthesized from the ion-exchanged catalyst grew from Ni particles (of very small size) lodged inside the pore system of the zeolite. Reaction temperature and C2H4/H2 (volume/volume) had a considerable effect on both carbon yield and CNFs morphol. Two types of CNFs were observed as a function of the reaction temperature: "fishbone structures" at temps. below 600° C and "tubular structures" at temps. above 600° C. On the other hand, as the C2H4/H2 ratio was decreased, the CNFs became slightly more graphitic in nature and the arrangement of graphite sheets changed from the fishbone structure to "octopus carbon".

CC 57-8 (Ceramics)

Section cross-reference(s): 78

OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS

RECORD (12 CITINGS)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2003:347304 HCAPLUS Full-text

DOCUMENT NUMBER: 139:56904

TITLE: Characterization and Catalytic Properties of

Titanium-Pillared Clays Prepared at Laboratory and

Pilot Scales: A Comparative Study

AUTHOR(S): Valverde, Jose L.; De Lucas, Antonio; Dorado,

Fernando; Sun-Kou, Rosario; Sanchez, Paula; Asencio, Isaac; Garrido, Agustín; Romero,

Amaya

CORPORATE SOURCE: Departamento de Ingenieria Quimica Facultad de

Quimicas, Universidad de Castilla-La Mancha, Ciudad

Real, 13004, Spain

SOURCE: Industrial & Engineering Chemistry Research (2003),

42(12), 2783-2790

CODEN: IECRED; ISSN: 0888-5885

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

The textural and structural characteristics and the acid properties of Ti-pillared montmorillonites prepared at bench scale (1 kg per batch level) have been compared with those prepared at laboratory scale (a few grams). The pillared clays have been examined by X-ray diffraction and characterized by different techniques and methods including nitrogen sorption isotherms, temperature-programmed desorption/reduction, and atomic absorption. The catalytic performance was evaluated by means of the selective reduction of NO by propylene over Cu2+ ion-exchanged samples. The differences of the textural characteristics between the laboratory and pilot samples did not significantly affect the catalytic results.

CC 59-3 (Air Pollution and Industrial Hygiene)

Section cross-reference(s): 67

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD

(6 CITINGS)

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2001:29927 HCAPLUS Full-text

DOCUMENT NUMBER: 134:265289

TITLE: Quality of olive oil. III. Application of

near-infrared spectroscopy (NIRS) to the quality

control of olive oil

AUTHOR(S): Garrido, A.; Sanchez Pineda de las

Infantas, M. T.; Cobo, C.

CORPORATE SOURCE: Depto. de Produccion Animal, Univ. de Cordoba, Spain

SOURCE: Alimentacion, Equipos y Tecnologia (2000), 19(7),

165-170

CODEN: AEQTDY; ISSN: 0212-1689

PUBLISHER: Editorial Alcion, S.A. DOCUMENT TYPE: Journal; General Review

LANGUAGE: Spanish

AB A review with 41 refs. The topics include current status of olive oil anal. and quality control, principles and instrumentation of NIRS, qual. and quant. anal. of olive oil by NIRS, and broader anal. applications to the anal. of oils and fats.

CC 17-0 (Food and Feed Chemistry)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2000:556213 HCAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 134:70432

TITLE: Olive oil quality. I. Concepts and analytical and

sensorial parameters of quality Sanchez Pineda, M. T.; Garrido, A.

; Cobo, C.

CORPORATE SOURCE: Dpt. de Bromatologia y Tecnologia de los Alimentos,

Universidad de Cordoba, Spain

SOURCE: Alimentacion, Equipos y Tecnologia (2000), 19(5),

63-69

CODEN: AEQTDY; ISSN: 0212-1689

PUBLISHER: Editorial Alcion, S.A. DOCUMENT TYPE: Journal; General Review

LANGUAGE: Spanish

AB A review with 21 refs. on the concept of olive oil quality, parameters of oil quality determined by traditional physicochem. methods, and olive oil quality parameters determined by organoleptic anal.

CC 17-0 (Food and Feed Chemistry)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L60 ANSWER 6 OF 7 WPIX COPYRIGHT 2010 THOMSON REUTERS on STN

ACCESSION NUMBER: 2008-D99595 [200828] WPIX

CROSS REFERENCE: 2008-E49165; 2008-E61270; 2008-G33820; 2008-L13777

DOC. NO. CPI: C2008-131560 [200828]

TITLE: Use of dihydroxybenzene compound to treat e.g. hemangiomas, hemangioblastomas, benign prostatic

hyperplasia, Barrett's disease, asthma, skeletal muscle

AUTHOR(S):

and tendon repair, Crohn's disease, ulcerative colitis

and leishmaniasis

DERWENT CLASS:

B05

INVENTOR: ANGULO FRUTOS J; CUEVAS SANCHEZ P; GIMENEZ GALLEGO G; LOZANO PUERTO R M; ROMERO GARRIDO A; SAENZ DE TEJADA

GORMAN I; VALVERDE LOPEZ S; LOPEZ S V;

FERNANDEZ JAEN T F; FRUTOS J A; MORENO NUNCIO F J; RIVAS

LOPEZ L I; SANCHEZ P C

PATENT ASSIGNEE: (ACTI-N) ACTION MEDICINES SL

COUNTRY COUNT: 120

PATENT INFO ABBR.:

PATENT NO	KIND DATE	WEEK LA	PG	MAIN IPC
WO 2008020034	A1 20080221	(200828)* EN	101[22]	

US 20080114063 A1 20080515 (200835) EN

APPLICATION DETAILS:

PATENT NO	KIND	API	PLICATION	DATE
WO 2008020034 A	A1	WO	2007-EP58447	7 20070815
US 20080114063	A1	US	2007-839529	20070815

PRIORITY APPLN. INFO: ES 2007-1855

20060816 ES 2006-2217

AB WO 2008020034 A1 UPAB: 20080501

> NOVELTY - Use of a 2,5-dihydroxybenzene compound (I) or its salt, solvate, isomer or prodrug in the manufacturing of a medicament for the treatment and/or prophylaxis of a disease of hemangiomas and hemangioblastomas, is claimed.

20070702

DETAILED DESCRIPTION - Use of a 2,5-dihydroxybenzene compound of formula (I) or its salt, solvate, isomer or prodrug in the manufacturing of a medicament for the treatment and/or prophylaxis of a disease of hemangiomas and hemangioblastomas, is claimed.

R1 = -(CH2)aY1 or -CH=CH-(CH2)pY1;

Y1 = -SO3H, -SO3-.X+, -SO3R3, -PO3H, -PO3-.X+, -PO3R3, -CO2H, -CO2-.X+ or -CO2R3;

X+ =organic cation or inorganic cation such that general charge of (I) is neutral;

R9, R9a = -OH or -OR2;

R2 = alkyl, aryl, alkylsulfonyl, arylsulfonyl, alkylcarbonyl or arylcarbonyl (all optionally substituted);

R3 = alkyl or aryl (both optionally substituted); and

a, p = 0-6.

ACTIVITY - Cytostatic; Gastrointestinal-Gen; Antiinflammatory; Antiasthmatic; Muscular-Gen; Osteopathic; Antiulcer; Protozoacide; Analgesic; Antiarthritic. MECHANISM OF ACTION - None given.

USE - (I) is useful for treating/preventing a disease of hemangiomas and hemangioblastomas (claimed), benign prostatic hyperplasia, Barrett's disease, asthma, skeletal muscle and tendon repair, Crohn's disease, ulcerative colitis (proctitis, proctosigmoiditis and pancolitis), leishmaniasis, pain and arthritis. The ability of (I) to treat muscle lesion was tested in a patient. The result showed that the patient (taken 500 mg of 2,5-dihydroxybenzene sulfonic acid for two weeks) recovered from the lesion in the quadriceps and the hematoma was not observed.

ADVANTAGE - (I) is safe and effective for treating leishmaniasis. (I) exhibits pharmacological properties.

CROSS REFERENCE: 2008-G33818; 2008-G33819; 2008-G33821; 2008-L13776

DOC. NO. CPI: C2008-188857 [200837]

TITLE: Use of 2,5-dihydroxybenzene derivatives to prepare a medicament for the therapeutic and/or prophylactic

treatment of e.g. skin cancer, prostate cancer, thyroid cancer, hematological dyscrasias and fibrosis (e.g.

endomyocardial fibrosis)

DERWENT CLASS: B05

INVENTOR: ROMERO GARRIDO A; ANGULO FRUTOS J; CUEVAS SANCHEZ P;

GIMENEZ GALLEGO G; LOZANO PUERTO R M; MORGAN I S D T; ROMERO GARRIDO A; SAENZ DE TEJADA GORMAN I; SAENZ DE TEJADA MORGAN I; VALVERDE LOPEZ S; VAVERDE LOPEZ S; DE

TEJADA M I S; FRUTOS J A; GALLEGO G G; GARRIDO A R; LOPEZ S V; LOZANO P R M;

SANCHEZ P C

PATENT ASSIGNEE: (ACTI-N) ACTION MEDICINES SL; (ACTI-N) ACTION MEDICINES

COUNTRY COUNT: 120

PATENT INFO ABBR.:

PA:	TENT NO	KINI	DATE	WEEK	LA	PG	MAIN IPC
WO	2008020027	A2	20080221	(200837)*	EN	86[15]	
US	20080113947	A1	20080515	(200837)	EN		
US	20080113948	A1	20080515	(200837)	EN		
US	20080114060	A1	20080515	(200837)	EN		
WO	2008020027	А3	20080410	(200837)	EN		
US	20080125486	A1	20080529	(200838)	EN		
ES	2315118	A1	20090316	(200922)	ES		
ES	2315118	В1	20091230	(201004)	ES		

APPLICATION DETAILS:

PATENT NO KIN	D Z	APPLICATION	DATE
WO 2008020027 A2	7	WO 2007-EP58440	20070815
ES 2315118 A1	I	ES 2006-2218 20	060816
US 20080113947 A1	Ţ	US 2007-839515	20070815
US 20080113948 A1	Ţ	US 2007-839520	20070815
US 20080114060 A1	Ţ	US 2007-839522	20070815
US 20080125486 A1	Ţ	US 2007-839525	20070815
ES 2315118 B1	I	ES 2006-2218 20	060816
PRIORITY APPLN. INFO: ES	2007-1856	20070702	
ES	2006-2218	20060816	

AB WO 2008020027 A2 UPAB: 20090407

NOVELTY - Use of 2,5-dihydroxybenzene derivatives (I) and their salts, solvate, isomer or prodrug to prepare a medicament for the therapeutic and/or prophylactic treatment of skin cancer, is claimed.

DETAILED DESCRIPTION - Use of a 2,5-dihydroxybenzene derivatives of formula (I) and their salts, solvate, isomer or prodrug to prepare a medicament for the therapeutic and/or prophylactic treatment of skin cancer, is claimed.

R1 = -(CH2)aY1 or -CH=CH-(CH2)pZ;

Y1 = -SO3H, -SO3-.X+, -SO3R3, -PO3H, -PO3-.X+, -PO3R3;

Z = -SO3H, -SO3-.X+, -SO3R3, -PO3H, -PO3-.X+, -PO3R3, -CO2H, -CO2-.X+ or -CO2R3;

X+= organic cation or inorganic cation, such that the general charge of the compound is neutral;

R9, R9a = OH or OR2;

R2 = alkyl, aryl, alkylsulfonyl, arylsulfonyl, alkylcarbonyl or arylcarbonyl (all optionally substituted);

R3 = alkyl or aryl (both optionally substituted); and a, p = 0-6.

Provided that: when Y1 is -SO3H, -SO3-.X+ or -SO3R3, then R9, R9a are OH or OR2; at least one of R9, R9a is alkylsulfonyloxy, arylsulfonyloxy, alkylcarbonyloxy or arylcarbonyloxy (all optionally substituted); and when R9, R9a are both OR2, then R9, R9a can be the same or different.

ACTIVITY - Cytostatic; Antianemic; Immunostimulant; Antiinflammatory. MECHANISM OF ACTION - Fibroblast mitogenesis inhibitor.

USE - (I) are useful to treat skin cancer such as lentigo maligna, melanoma, keratoacanthoma, basal cell carcinoma, squamous cell carcinoma, Merkel cell carcinoma, sarcoma, angiosarcoma, cutaneous lymphoma, sweat gland carcinoma and sebaceous gland carcinoma (claimed). (I) are useful to treat hematological dyscrasias, myelodysplastic syndromes or fibrosis (e.g. endomyocardial fibrosis, idiopathic pulmonary fibrosis, pulmonary fibrosis, progressive massive fibrosis and renal interstitial fibrosis). (I) are useful for improving the efficacy of chemotherapy, radiation therapy and/or cancer immunotherapy. (I) is useful for the treatment/prophylaxis of cancer of an organ (e.g. breast cancer, bladder cancer, colon cancer, rectal cancer, kidney cancer, lung cancer, cervical cancer, prostate cancer, brain cancer, testicular cancer, thyroid cancer and ovarian cancer). The ability of (I) to treat prostate cancer was tested in mice. The result showed that the percentage of control of prostate cancer by 2,5-diacetoxybenzene sulfonate was 85% and 72%, at 1 mu M and 5 mu M, respectively.

ADVANTAGE - (I) are effective for treating fibrosis and cancer.

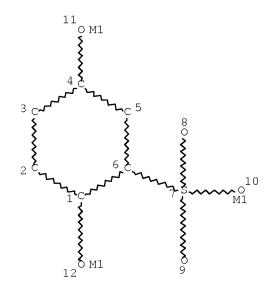
STRUCTURE SEARCH

=> FILE HCAPLUS

FILE 'HCAPLUS' ENTERED AT 17:22:51 ON 22 JUL 2010
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=> D STAT QUE L23

L2 STR



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HCOUNT IS M1 AT 10
HCOUNT IS M1
             AT 11
HCOUNT IS M1
             AT 12
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NSPEC
             ΑT
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              ΑT
     IS R
             ΑT
                 3
NSPEC
    IS R
            AT 4
AT 5
NSPEC
NSPEC IS R
NSPEC IS R
             ΑT
NSPEC IS C
             AT 7
             AT
NSPEC IS C
                 8
                 9
     IS C
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NSPEC
     IS C
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NSPEC
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             AT 11
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

NODE ATTRIBUTES:

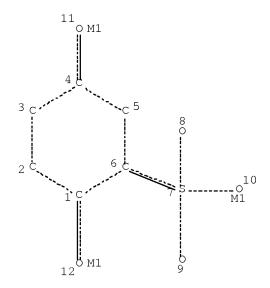
RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

L4 575 SEA FILE=REGISTRY SSS FUL L2

L5 STR

Page 10 of 46



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NODE ATTRIBUTES:
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                    11
HCOUNT
                 AΤ
HCOUNT
       IS M1
                 ΑT
                    12
NSPEC
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                 ΑT
NSPEC
       IS R
                 AT
       IS R
                      3
NSPEC
                 ΑT
       IS R
NSPEC
                 AT
                      4
NSPEC
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                 ΑT
                      5
NSPEC
       IS R
                 AT
                      6
                      7
NSPEC
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                ΑT
NSPEC
      IS C
                ΑT
                      8
       IS C
NSPEC
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       IS C
NSPEC
                 AT 10
NSPEC
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                 ΑT
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NSPEC
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                 ΑT
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MLEVEL IS CLASS AT
                    7 8 9 10 11 12
DEFAULT ECLEVEL IS LIMITED
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GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE L7 569 SEA FILE=REGISTRY SUB=L4 SSS FUL L5 L8 1313 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L7 L9 21558 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON PSORIASIS+PFT/CT OR (?PSORIASIS? OR ?PUSTULOSIS?)/BI L10 6 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L8 AND L9 L11 553 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L8 AND ((BAC OR DMA OR PAC OR PKT OR THU)/RL OR (?THERA? OR ?PHARM? OR ?DRUG? OR ?TREAT?)/BI) L12 6 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L11 AND L9 6 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L10 OR L12 L13 1 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON "2,5-DIHYDROXYBENZENE L14 SULFONIC ACID"/CN L15 181 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L14 L16 68 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L15 AND ((BAC OR DMA

Page 11 of 46

L23	6 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L22 OR L18
L22	4 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L21 AND L9
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	OR PAC OR PKT OR THU)/RL OR (?THERA? OR ?PHARM? OR ?DRUG? OR
L21	359 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L20 AND ((BAC OR DMA
L20	494 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L19
	IC ACID SODIUM SALT"/CN)
	MONOTOSYLATE MORPHOLINE SALT"/CN OR "2,5-DIHYDROXYBENZENESULFON
	ACID MONOSODIUM SALT"/CN OR "2,5-DIHYDROXYBENZENESULFONIC ACID
	C ACID DIETHYLAMINE SALT"/CN OR "2,5-DIHYDROXYBENZENESULFONIC
	ESULFONIC ACID CALCIUM SALT"/CN OR "2,5-DIHYDROXYBENZENESULFON
L19	4 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON ("2,5-DIHYDROXYBENZEN
L18	6 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L13 OR L17
L17	5 SEA FILE=HCAPLUS SPE=ON ABB=ON PLU=ON L16 AND L9
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	OR PAC OR PKT OR THU)/RL OR (?THERA? OR ?PHARM? OR ?DRUG? OR

=> S L23 NOT L33

L61 6 L23 NOT L33

=> FILE WPIX

FILE 'WPIX' ENTERED AT 17:23:02 ON 22 JUL 2010 COPYRIGHT (C) 2010 THOMSON REUTERS

FILE LAST UPDATED: 21 JUL 2010 <20100721/UP>
MOST RECENT UPDATE: 201046 <201046/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE >>> Now containing more than 1.6 million chemical structures in DCR <<<

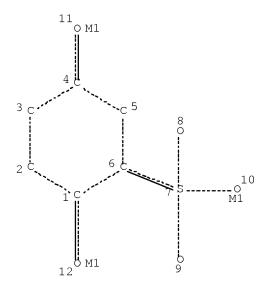
222 Now Concurring more chair 1.0 million chamical belaced in Bolt

>>> IPC, ECLA, US National Classifications and Japanese F-Terms and FI-Terms have been updated with reclassifications to end of March 2010.

No update date (UP) has been created for the reclassified documents, but they can be identified by specific update codes (see HELP CLA for details) <<<

=> D STAT QUE L40

L5 STR



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Serial#: 10/588,166
NODE ATTRIBUTES:
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      IS
      M1
      AT
      11

      HCOUNT
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NSPEC IS C
                       AT 11
NSPEC IS C AT 12
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MLEVEL IS CLASS AT 7 8 9 10 11 12
DEFAULT ECLEVEL IS LIMITED
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NUMBER OF NODES IS 12
STEREO ATTRIBUTES: NONE
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L39
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=> S L40 NOT L52
                  4 L40 NOT L52
L62
=> DUP REMOVE L61 L62
FILE 'HCAPLUS' ENTERED AT 17:23:38 ON 22 JUL 2010
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'WPIX' ENTERED AT 17:23:38 ON 22 JUL 2010
COPYRIGHT (C) 2010 THOMSON REUTERS
PROCESSING COMPLETED FOR L61
PROCESSING COMPLETED FOR L62
                   8 DUP REMOVE L61 L62 (2 DUPLICATES REMOVED)
L63
                      ANSWERS '1-6' FROM FILE HCAPLUS
                      ANSWERS '7-8' FROM FILE WPIX
L63 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2010 ACS on STN DUPLICATE 1
ACCESSION NUMBER:
                                  2008:221788 HCAPLUS Full-text
DOCUMENT NUMBER:
                                  148:276732
TITLE:
                                  Use of 2,5-dihydroxybenzene derivatives for the
                                  treatment of arthritis and pain
INVENTOR(S):
                                  Cuevas Sanchez, Pedro; Gimenez Gallego, Guillermo;
                                  Saenz de Tejada Gorman, Inigo; Angulo Frutos, Javier;
                                  Lozano Puerto, Rosa Maria; Romero Garrido, Antonio;
                                  Valverde Lopez, Serafin
PATENT ASSIGNEE(S):
                               Action Medicines, S.L., Spain
                                  PCT Int. Appl., 134pp.
```

CODEN: PIXXD2

Patent

Page 13 of 46

DOCUMENT TYPE:

SOURCE:

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

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PATENT NO.
                  KIND DATE APPLICATION NO. DATE
     WO 2008020033 A1
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             KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
             MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
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             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
     ES 2315117 A1 20090316 ES 2006-2217 ES 2315117 B1 20091230
                                                                   20060816
     US 20080114063 A1 20080515 US 2007-839529 20070815 EP 2054045 A1 20090506 EP 2007-788431 20070815
         R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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             AL, BA, HR, MK, RS
                                            ES 2006-2217 A 20060816
ES 2007-1855 A 20070702
PRIORITY APPLN. INFO.:
                                            WO 2007-EP58446 W 20070815
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 148:276732
      The present invention relates to the use of 2,5-dihydroxybenzene derivs. or
pharmaceutically acceptable salt or solvate, isomer or prodrug thereof in the
manufacturing of a medicament for the treatment and/or prophylaxis of arthritis and pain.
IPCI A61K0031-10 [I,A]; A61K0031-095 [I,C*]; A61K0031-192 [I,A]; A61K0031-185
     [I,C^*]; A61P0019-02 [I,A]; A61P0019-00 [I,C^*]; A61K0031-618 [I,A];
     A61K0031-60 [I,A]
IPCR A61K0031-095 [I,C]; A61K0031-10 [I,A]; A61K0031-185 [I,C]; A61K0031-192
     [I,A]; A61K0031-60 [I,C]; A61K0031-60 [I,A]; A61K0031-618 [I,A];
     A61P0019-00 [I,C]; A61P0019-02 [I,A]
CC
     1-7 (Pharmacology)
     Section cross-reference(s): 63
ST
     hydroxybenzene deriv arthritis pain therapy
ΤT
     Hepatocyte growth factor
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (antagonists; use of hydroxybenzene derivs. for treatment of
        arthritis and pain)
ΙT
     Angiogenesis
        (corneal; use of hydroxybenzene derivs. for treatment of
        arthritis and pain)
     Blood vessel, neoplasm
ΙT
        (hemangioblastoma; use of hydroxybenzene derivs. for treatment
        of arthritis and pain)
ΤТ
     Respiratory system disease
        (hyperresponsiveness; use of hydroxybenzene derivs. for
        treatment of arthritis and pain)
     Helicobacter pylori
ΙT
        (infection; use of hydroxybenzene derivs. for treatment of
        arthritis and pain)
     Pharmaceutical injections
ΙT
        (intraarticular; use of hydroxybenzene derivs. for treatment
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Serial#: 10/588,166
        of arthritis and pain)
ΤТ
     Protozoacides
        (leishmanicides; use of hydroxybenzene derivs. for treatment
        of arthritis and pain)
ΙT
     Skeletal muscle
        (lesions; use of hydroxybenzene derivs. for treatment of
        arthritis and pain)
     Arthritis
ΙT
        (lupus-related, psoriasis-related, infectious, viral,
        parasitic, bacterial; use of hydroxybenzene derivs. for
        treatment of arthritis and pain)
ΙT
     Fibroblast
        (mitogenesis; use of hydroxybenzene derivs. for treatment of
        arthritis and pain)
ΙT
     Leukotrienes
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (modifiers; use of hydroxybenzene derivs. for treatment of
        arthritis and pain)
ΙT
     Arthritis
        (polyarthritis; use of hydroxybenzene derivs. for treatment
        of arthritis and pain)
ΙT
     Disease, animal
        (pterygium; use of hydroxybenzene derivs. for treatment of
        arthritis and pain)
     Proliferation inhibition
ΙT
        (retinal endothelial; use of hydroxybenzene derivs. for
        treatment of arthritis and pain)
ΙT
     Interleukin receptors
     RL: PAC (Pharmacological activity); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (solubilized; use of hydroxybenzene derivs. for treatment of
        arthritis and pain)
     Pharmaceutical emulsions
ΤТ
     Topical drug delivery systems
        (topical lotions; use of hydroxybenzene derivs. for treatment
        of arthritis and pain)
     Analgesics
ΙT
     Anesthetics
     Angiogenesis inhibitors
     Anti-inflammatory agents
     Antiandrogens
     Antiarthritics
     Antiasthmatics
     Antibiotics
     Antioxidants
     Antirheumatic agents
     Antitumor agents
     Asthma
     Buccal drug delivery systems
     Cholinergic antagonists
     Crohn disease
     Endometriosis
     Gastroenteritis
     Gout
     Hemangioma
     Human
     Immunomodulators
     Immunosuppressants
     Inhalation drug delivery systems
     Leishmaniasis
     Neuroglia, neoplasm
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Serial#: 10/588,166 Nonsteroidal anti-inflammatory drugs Ophthalmic drug delivery systems Oral drug delivery systems Osteoarthritis Otic drug delivery systems Pain Parasiticides Parenteral drug delivery systems Pharmaceutical creams Pharmaceutical gels Pharmaceutical solids Pharmaceutical solutions Prodrugs Prophylaxis Rectal drug delivery systems Rheumatoid arthritis Topical drug delivery systems Transdermal drug delivery systems Ulcerative colitis Vaginal drug delivery systems α -Adrenoceptor antagonists β -Adrenoceptor agonists (use of hydroxybenzene derivs. for treatment of arthritis and pain) Corticosteroids ΙT RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (use of hydroxybenzene derivs. for treatment of arthritis and pain) 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor ΙT 127464-60-2, Vascular endothelial growth factor RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; use of hydroxybenzene derivs. for treatment of arthritis and pain) ΙT 7440-57-5, Gold, biological studies RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (i.m.; use of hydroxybenzene derivs. for treatment of arthritis and pain) 9081-34-9, 5- α -Reductase ΙT RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; use of hydroxybenzene derivs. for treatment of arthritis and pain) 106096-92-8, FGF-1 ΤТ RL: BSU (Biological study, unclassified); BIOL (Biological study) (use of hydroxybenzene derivs. for treatment of arthritis and pain) 88-46-0, 2,5-Dihydroxybenzenesulfonic acid 88-46-0D, ΙT 2,5-Dihydroxybenzenesulfonic acid, ester derivs. 2,5-Dihydroxycinnamic acid 21799-87-1, Potassium 2,5-dihydroxybenzenesulfonate 28088-64-4D, Aminosalicylic acid, derivs. 51579-69-2 57775-26-5 59687-22-8 60630-38-8 63177-57-1 79122-68-2 159252-66-1 159252-66-1D, ester derivs. 748106-93-61007839-71-5 1007839-72-6D, ester derivs. 1007839-87-3 1007839-89-5 1007839 - 91 - 9 1007839 - 93 - 1 1007839 - 94 - 2 1007839 - 96 - 4 1007840 - 16 - 51007840 - 17 - 6 1007840 - 18 - 7 1007840 - 19 - 8 1007840 - 20 - 1 1007840 - 21 - 21007840-22-3 1007840-23-4 1007840-24-5 1007849-27-5RL: PAC (Pharmacological activity); THU (Therapeutic

(use of hydroxybenzene derivs. for treatment of arthritis and

use); BIOL (Biological study); USES (Uses)

pain)

IT 88-46-0, 2,5-Dihydroxybenzenesulfonic acid 88-46-0D,
2,5-Dihydroxybenzenesulfonic acid, ester derivs. 21799-87-1,
Potassium 2,5-dihydroxybenzenesulfonate
RL: PAC (Pharmacological activity); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(use of hydroxybenzene derivs. for treatment of arthritis and pain)

RN 88-46-0 HCAPLUS
CN Benzenesulfonic acid, 2,5-dihydroxy- (CA INDEX NAME)

RN 88-46-0 HCAPLUS CN Benzenesulfonic acid, 2,5-dihydroxy- (CA INDEX NAME)

RN 21799-87-1 HCAPLUS
CN Benzenesulfonic acid, 2,5-dihydroxy-, potassium salt (1:1) (CA INDEX NAME)

● K

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2010 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2005:888919 HCAPLUS Full-text

DOCUMENT NUMBER: 143:216719

TITLE: Use of 2,5-dihydroxybenzenesulfonic acid in the

production of medicaments for the treatment

of angiodependent diseases such as cancer and

psoriasis

INVENTOR(S): Cuevas, Sanchez Pedro

PATENT ASSIGNEE(S): Investread Europa, S.L., Spain

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Spanish

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

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		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS	S, 1	JP,	ΚE,	KG,	KP,	KR	, KZ,	LC,
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		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU	J,	SC,	SD,	SE,	SG,	SK	, SL,	SY,
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US	2008	0293	816		A1		2008	1127		US	20	08-	5881	66			20080	807
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										US	20	08-	5881	66		A2 :	20080	807
SIGNM	ENT H	ISTO	RY F	OR U	S PA'	TENT	AVA	ILAB:	LE I	N L	SU	S D	ISPL	AY F	ORMA	Τ		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to the use of 2,5-dihydroxybenzenesulfonic acid in the production of medicaments for the treatment of angiodependent diseases. More specifically, the invention relates to the use of the aforementioned compound and, in particular, the calcium and potassium salts thereof, for the treatment of two angiodependent diseases which present a reduction in apoptosis, namely cancer and psoriasis. The invention also discloses the antiproliferative, antimigratory, antiangiogenic and proapoptotic capacity of said family of compds. in non-quiescent

known cytostatic medicines in the treatment of tumors and, specifically, on gliomas. The invention further relates to the therapeutic efficacy of said compds., based on the combined antiproliferative, antiangiogenic and proapoptotic capacities thereof, in the treatment of chronic psoriatic plaques. IPCI A61K0031-185 [ICM, 7]; A61P0035-00 [ICS, 7]; A61P0017-06 [ICS, 7]; A61P0017-00 [ICS, 7, C*] IPCR A61K0031-185 [I,C*]; A61K0031-185 [I,A]; A61K0031-21 [I,C*]; A61K0031-255 [I,A]; A61P0017-00 [I,C*]; A61P0017-06 [I,A]; A61P0035-00 [I,C*]; A61P0035-00 [I,A] CC 63-6 (Pharmaceuticals) ST dihydroxybenzenesulfonic acid drug formulation ΙT Neoplasm Psoriasis (use of dihydroxybenzenesulfonic acid in drugs for treatment of angiodependent diseases) 88-46-0, 2,5-Dihydroxybenzenesulfonic acid 20123-80-2 ΙT , 2,5-Dihydroxybenzenesulfonic acid calcium salt 862162-74-1 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (use of dihydroxybenzenesulfonic acid in drugs for treatment of angiodependent diseases) 88-46-0, 2,5-Dihydroxybenzenesulfonic acid 20123-80-2 ΙT , 2,5-Dihydroxybenzenesulfonic acid calcium salt 862162-74-1 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (use of dihydroxybenzenesulfonic acid in drugs for treatment of angiodependent diseases) 88-46-0 HCAPLUS RN CN Benzenesulfonic acid, 2,5-dihydroxy- (CA INDEX NAME)

cells. In addition, the invention details the potentiating effect of said compds. on

RN 20123-80-2 HCAPLUS CN Benzenesulfonic acid, 2,5-dihydroxy-, calcium salt (2:1) (CA INDEX NAME)

 $\bigcirc 1/2$ Ca

RN 862162-74-1 HCAPLUS
CN Benzenesulfonic acid, 2,5-dihydroxy-, potassium salt (1:?) (CA INDEX NAME)



•x K

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD

(3 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:521020 HCAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 150:487712

TITLE: Methods of use 2,5-dihydroxybenzene sulfonic acid

compounds for the treatment of cancer,

rosacea and psoriasis

INVENTOR(S): Cuevas Sanchez, Pedro; Romero Garrido, Antonio;

Gimenez Gallego, Guillermo; Valverde Lopez, Serafin;

Lozano Puerto, Rosa Maria

PATENT ASSIGNEE(S): Action Medicines, S.L., Spain

SOURCE: U.S. Pat. Appl. Publ., 32pp., Cont.-in-part of U.S.

Ser. No. 588,166.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PA.	TENT :	NO.			KIN	D	DATE		•	APP	LICAT	ION :	NO.		D.	ATE	
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WO	2005	0773	52		A1		2005	0825		WO	2005-	ES70	017		2	0050	216
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB	, BG,	BR,	BW,	BY,	BZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ	, EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS	, JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG	, MK,	MN,	MW,	MX,	MZ,	NA,	NI,
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU	, SC,	SD,	SE,	SG,	SK,	SL,	SY,
		ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US	, UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW
	RW:	BW,	GH,	GM,	KΕ,	LS,	MW,	MZ,	NA,	SD	, SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
		ΑZ,	BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM,	ΑT	, BE,	BG,	CH,	CY,	CZ,	DE,	DK,
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IS	, IT,	LT,	LU,	MC,	NL,	PL,	PT,
		RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG	, CI,	CM,	GA,	GN,	GQ,	GW,	ML,
		MR,	NE,	SN,	TD,	ΤG											
US	2007	0149	618		A1		2007	0628		US	2006-	5064	69		2	0060	816
US	2008	0293	816		A1		2008	1127		US	2008-	5881	66		2	0800	807
PRIORIT	Y APP	LN.	INFO	.:						ES	2004-	371			A 2	0040	217
										WO	2005-	ES70	017	1	W 2	0050	216
										US	2006-	5064	69		A3 2	0060	816
										US	2008-	5881	66		A2 2	0800	807
										US	2006-	5881	66	1	A2 2	0060	802

GI

AB Methods of use 2,5-dihydroxybenzene sulfonic acid compds. of formula I, where X is a hydrogen, an organic cation or an inorg. cation; n is an integer from 1 to 2; and m is an integer from 1 to 2, for the treatment of cancer, rosacea and psoriasis are disclosed. The invention describes compns. and methods of use for 2,5dihydroxybenzene sulfonic acid compds. and pharmaceutically acceptable salts thereof. The invention provides methods for the treatment of skin cancer, organ cancer and leukemia. Method also involves in improving the efficacy of chemotherapy, radiation therapy and cancer immunotherapy. The invention also provides methods for the treatment of rosacea and psociasis by administration of a composition comprising at least one 2,5-dihydroxybenzene sulfonic acid compound or a pharmaceutically acceptable salt thereof, and, optionally at least one other therapeutic agent. In the invention the 2,5-dihydroxybenzene sulfonic acid compds. or pharmaceutically acceptable salts thereof are 2,5-dihydroxybenzene sulfonic acid, calcium 2,5-dihydroxybenzenesulfonate, potassium 2,5-dihydroxybenzenesulfonate, magnesium 2,5-dihydroxybenzenesulfonate and diethylamine 2,5dihydroxybenzenesulfonate. INCL 514167000; 514576000; 514568000; 514171000 IPCI A61K0031-59 [I,A]; A61K0031-185 [I,A]; A61K0031-192 [I,A]; A61K0031-56 [I,A]; A61P0035-00 [I,A]; A61P0017-00 [I,A] IPCR A61K0031-59 [I,C]; A61K0031-59 [I,A]; A61K0031-185 [I,C]; A61K0031-185 [I,A]; A61K0031-192 [I,A]; A61K0031-56 [I,C]; A61K0031-56 [I,A]; A61P0017-00 [I,C]; A61P0017-00 [I,A]; A61P0035-00 [I,C]; A61P0035-00 [I,A] NCL 514/167.000; 514/171.000; 514/568.000; 514/576.000 1-6 (Pharmacology) CC Section cross-reference(s): 2, 63 dihydroxybenzene sulfonate compd steroid combination therapy ST cancer rosacea psoriasis; antitumor antiinflammatory antioxidant combination chemotherapy potentiation dihydroxybenzene sulfonate compd ΙT Animal cell line (C-6; methods of use 2,5-dihydroxybenzene sulfonic acid compds. for treatment of cancer, rosacea and psoriasis) Skin, neoplasm ΤТ (basal cell carcinoma; methods of use 2,5-dihydroxybenzene sulfonic acid compds. for treatment of cancer, rosacea and psoriasis) ΤT Carcinoma (basal cell; methods of use 2,5-dihydroxybenzene sulfonic acid compds. for treatment of cancer, rosacea and psoriasis) Anti-inflammatory agents ΙT

(codrugs; methods of use 2,5-dihydroxybenzene sulfonic acid

compds. for treatment of cancer, rosacea and

IT Retinoids Steroids

Antimicrobial agents

Antioxidants

psoriasis)

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Serial#: 10/588,166
     RL: PAC (Pharmacological activity); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (codrugs; methods of use 2,5-dihydroxybenzene sulfonic acid
        compds. for treatment of cancer, rosacea and
        psoriasis)
ΙT
    Antiproliferative agents
     Antitumor agents
     Brain, neoplasm
     Combination chemotherapy
     Erythema
     Human
     Leukemia
    Melanoma
    Neoplasm
     Neuroglia, neoplasm
       Pharmaceutical carriers
       Pharmaceutical creams
       Psoriasis
     Skin, neoplasm
     Telangiectasia
     Topical drug delivery systems
        (methods of use 2,5-dihydroxybenzene sulfonic acid compds. for
        treatment of cancer, rosacea and psoriasis)
ΙT
     Hydrocarbon oils
     Petrolatum
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (methods of use 2,5-dihydroxybenzene sulfonic acid compds. for
        treatment of cancer, rosacea and psoriasis)
ΙT
     Drug interactions
        (potentiation; methods of use 2,5-dihydroxybenzene sulfonic acid
        compds. for treatment of cancer, rosacea and
        psoriasis)
     Skin, disease
ΤT
        (rosacea, characterized by papules and pustules; methods of use
        2,5-dihydroxybenzene sulfonic acid compds. for treatment of
        cancer, rosacea and psoriasis)
ΙT
     Skin, disease
        (rosacea; methods of use 2,5-dihydroxybenzene sulfonic acid compds. for
        treatment of cancer, rosacea and psoriasis)
     Neuroglia, neoplasm
ΤT
        (s.c.; methods of use 2,5-dihydroxybenzene sulfonic acid compds. for
        treatment of cancer, rosacea and psoriasis)
     69-72-7, Salicylic acid, biological studies
ΙT
     RL: PAC (Pharmacological activity); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (codrug; methods of use 2,5-dihydroxybenzene sulfonic acid
        compds. for treatment of cancer, rosacea and
       psoriasis)
     1406-16-2D, Vitamin D, analogs
     RL: PAC (Pharmacological activity); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (codrugs; methods of use 2,5-dihydroxybenzene sulfonic acid
        compds. for treatment of cancer, rosacea and
        psoriasis)
     51-21-8, 5-FU
                    57-22-7, Vincristine 88-46-0,
     2,5-Dihydroxybenzene sulfonic acid 2624-44-4, Diethylamine
     2,5-dihydroxybenzenesulfonate 15663-27-1, Cisplatin 20123-80-2
     , Calcium 2,5-dihydroxybenzenesulfonate 21799-87-1, Potassium
     2,5-dihydroxybenzenesulfonate 33069-62-4, Paclitaxel 97225-83-7,
     Magnesium 2,5-dihydroxybenzenesulfonate 97682-44-5, Irinotecan
     RL: PAC (Pharmacological activity); THU (Therapeutic
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Serial#: 10/588,166
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use); BIOL (Biological study); USES (Uses) (methods of use 2,5-dihydroxybenzene sulfonic acid compds. for treatment of cancer, rosacea and psoriasis) ΙT 112-92-5, Stearyl alcohol 36653-82-4, Cetyl alcohol RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (methods of use 2,5-dihydroxybenzene sulfonic acid compds. for treatment of cancer, rosacea and psoriasis) 88-46-0, 2,5-Dihydroxybenzene sulfonic acid 2624-44-4 , Diethylamine 2,5-dihydroxybenzenesulfonate 20123-80-2, Calcium 2,5-dihydroxybenzenesulfonate 21799-87-1, Potassium 2,5-dihydroxybenzenesulfonate RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (methods of use 2,5-dihydroxybenzene sulfonic acid compds. for treatment of cancer, rosacea and psoriasis) 88-46-0 HCAPLUS RN Benzenesulfonic acid, 2,5-dihydroxy- (CA INDEX NAME) CN

RN 2624-44-4 HCAPLUS
CN Benzenesulfonic acid, 2,5-dihydroxy-, compd. with N-ethylethanamine (1:1)
(CA INDEX NAME)

CM 1

CRN 109-89-7

CMF C4 H11 N

H3C-CH2-NH-CH2-CH3

CRN 88-46-0 CMF C6 H6 O5 S

RN

Benzenesulfonic acid, 2,5-dihydroxy-, calcium salt (2:1) (CA INDEX NAME)

1/2 Ca

21799-87-1 HCAPLUS RN

Benzenesulfonic acid, 2,5-dihydroxy-, potassium salt (1:1) (CA INDEX CN

L63 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER:

2008:1162068 HCAPLUS Full-text

DOCUMENT NUMBER: 149:402057

Nitrosated derivatives of 2,5-dihydroxybenzene TITLE:

compounds and their preparation and use in the

treatment of diseases

INVENTOR(S): Gimenez Gallego, Guillermo; Saenz De Tejada Gorman,

Inigo; Cuevas Sanchez, Pedro; Angulo Frutos, Javier;

Valverde Lopez, Serafin

PATENT ASSIGNEE(S): Action Medicines, S.L., Spain

SOURCE: PCT Int. Appl., 147pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE	E APPLICAT	APPLICATION NO.				
WO 2008113863 WO 2008113863		 80925 WO 2008- 81211	-EP53455	20080324			
W: AE, AG, AL, CA, CH, CN, FI, GB, GD, KG, KM, KN, ME, MG, MK,	AM, AO, AT, CO, CR, CU, GE, GH, GM, KP, KR, KZ, MN, MW, MX,	, AU, AZ, BA, BB, , CZ, DE, DK, DM, , GT, HN, HR, HU, , LA, LC, LK, LR, , MY, MZ, NA, NG, , SD, SE, SG, SK,	DO, DZ, EC, ID, IL, IN, LS, LT, LU, NI, NO, NZ,	EE, EG, ES, IS, JP, KE, LY, MA, MD, OM, PG, PH,			

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TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO:

ES 2007-2037 A 20070720

OTHER SOURCE(S):
CASREACT 149:402057; MARPAT 149:402057
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$$\mathbb{R}^{9}$$
 \mathbb{I}
 \mathbb{R}^{9}
 \mathbb{I}
 \mathbb{R}^{9}

The invention relates to nitrosated derivs. of 2,5-dihydroxybenzene compds. of formula I that are useful in the preparation of medicinal products for the treatment of different diseases. The diseases in question are, in particular: cancer, rosacea, psoriasis, fibrosis, hemangiomas, ocular diseases, skin pigmentation and skin hyperpigmentation, diseases associated with amyloidosis, dermatitis, actinic and seborrheic keratosis, erectile dysfunction, female sexual dysfunction, arterial hypertension, atherosclerosis, inflammatory diseases in particular, arthritis, glomerulonephritis and asthma, intestinal inflammatory diseases in particular, ulcerative colitis and Crohn's disease, benign prostatic hyperplasia, Leishmaniasis, angiogenesis associated to chronic temporal lobe epilepsy, pain, hyperlipidemia and thrombosis. Compds. of formula I wherein R1 is (CH2)0-6SO3H and derivs., (CH2)0-6PO3H and derivs., (CH2)0-6CO2H and derivs., CH=CH(CH2)0-6SO3H and derivs., CH=CH(CH2)0-6PO3H and derivs., and CH=CH(CH2)0-6CO2H and derivs.; R9 and R9' are independently OH and derivs. and Oacyl, with the proviso that at least one of R9 and R9' is OH derivative; and their salts, isomers, prodrugs and solvates thereof, are claimed. Example compound II was prepared by esterification of 5-bromovaleric acid with 4-nitrophenol; the resulting 5-bromovaleric acid 4-nitrophenyl ester underwent nitrosation with silver nitrate to give 5nitrooxyvaleric acid 4-nitrophenyl ester, which underwent sulfonylation and substitution to give compound II. All the invention compds. were evaluated for their FGF-1 inhibitory activity (data given).

IPCI C07C0203-04 [I,A]; C07C0309-24 [I,A]; C07C0309-42 [I,A]; A61K0031-216 [I,A]; A61K0031-215 [I,A]; A61P0035-00 [I,A]; A61P0001-04 [I,A]; A61P0015-10 [I,A]; A61P0015-12 [I,A]; A61P0017-06 [I,A]; A61P0025-08 [I,A]; A61P0019-02 [I,A]; A61P0027-02 [I,A]; A61P0029-00 [I,A]; A61P0007-02 [I,A]; A61P0007-04 [I,A]; A61P0009-12 [I,A]; A61P0009-00 [I,C*]; C07C0203-00 [I,C]; C07C0203-04 [I,A]; A61K0031-21 [I,C]; A61K0031-215 [I,A]; A61K0031-216 [I,A]; A61P0001-00 [I,C]; A61P0001-04 [I,A]; A61P0007-00 [I,C]; A61P0007-02 [I,A]; A61P0015-00 [I,C]; A61P0015-10 [I,A]; A61P0015-12 [I,A]; A61P0017-00 [I,C]; A61P0017-06 [I,A]; A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0025-00 [I,C]; A61P0025-08 [I,A]; A61P0027-00 [I,C]; A61P0027-02 [I,A]; A61P0029-00 [I,C]; A61P0029-00 [I,A]; A61P0035-00 [I,C]; A61P0035-00 [I,A]; C07C0309-00 [I,C]; C07C0309-24 [I,A]; C07C0309-42 [I,A] IPCR C07C0203-00 [I,C]; C07C0203-04 [I,A]; A61K0031-21 [I,C]; A61K0031-215 [I,A]; A61K0031-216 [I,A]; A61P0001-00 [I,C]; A61P0001-04 [I,A]; A61P0007-00 [I,C]; A61P0007-02 [I,A]; A61P0015-00 [I,C]; A61P0015-10 [I,A]; A61P0015-12 [I,A]; A61P0017-00 [I,C]; A61P0017-06 [I,A];

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Serial#: 10/588,166
     A61P0019-00 [I,C]; A61P0019-02 [I,A]; A61P0025-00 [I,C]; A61P0025-08
     [I,A]; A61P0027-00 [I,C]; A61P0027-02 [I,A]; A61P0029-00 [I,C];
     A61P0029-00 [I,A]; A61P0035-00 [I,C]; A61P0035-00 [I,A]; C07C0309-00
     [I,C]; C07C0309-24 [I,A]; C07C0309-42 [I,A]
CC
     25-13 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
     Section cross-reference(s): 1, 63
    nitrosated dihydroxybenzenesulfonic acid prepn FGF1 inhibitor
ST
     treatment disease
ΙT
    Amyloidosis
        (- associated diseases, treatment of; preparation of nitrosated
        derivs. of dihydroxybenzene compds. useful in treatment and
        prophylaxis of different diseases)
ΤТ
    Animal cell line
        (3T3; preparation of nitrosated derivs. of dihydroxybenzene compds. useful
        in treatment and prophylaxis of different diseases)
ΤТ
     Keratosis
        (actinic, treatment of; preparation of nitrosated derivs. of
        dihydroxybenzene compds. useful in treatment and prophylaxis
        of different diseases)
    Antiarteriosclerotics
ΤТ
        (antiatherosclerotics; preparation of nitrosated derivs. of dihydroxybenzene
        compds. useful in treatment and prophylaxis of different
        diseases)
     Prostate gland disease
ΤТ
        (benign hyperplasia, treatment of; preparation of nitrosated
        derivs. of dihydroxybenzene compds. useful in treatment and
        prophylaxis of different diseases)
ΙT
    Angiogenesis
        (chronic temporal lobe epilepsy- associated, treatment of;
        preparation of nitrosated derivs. of dihydroxybenzene compds. useful in
        treatment and prophylaxis of different diseases)
ΙT
    Antimicrobial agents
     Antioxidants
     Cholinesterase inhibitors
     Endothelin receptor antagonists
     Immunomodulators
     NMDA receptor antagonists
     Nonsteroidal anti-inflammatory drugs
        (codrugs; preparation of nitrosated derivs. of dihydroxybenzene
        compds. useful in treatment and prophylaxis of different
       diseases)
ΙT
    Retinoids
     Steroids
     RL: PAC (Pharmacological activity); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (codrags; preparation of nitrosated derivs. of dihydroxybenzene
        compds. useful in treatment and prophylaxis of different
        diseases)
ΙT
    Hydrolysis
        (enzymic; preparation of nitrosated derivs. of dihydroxybenzene compds.
        useful in treatment and prophylaxis of different diseases)
ΙT
     Sexual disorders
        (female, treatment of; preparation of nitrosated derivs. of
        dihydroxybenzene compds. useful in treatment and prophylaxis
        of different diseases)
    Cell proliferation
ΙT
        (glioma; preparation of nitrosated derivs. of dihydroxybenzene compds.
        useful in treatment and prophylaxis of different diseases)
ΙT
     Skin, disease
        (hyperpigmentation, treatment of; preparation of nitrosated
        derivs. of dihydroxybenzene compds. useful in treatment and
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Serial#: 10/588,166
        prophylaxis of different diseases)
TT
     Sexual disorders
        (impotence, treatment of; preparation of nitrosated derivs. of
        dihydroxybenzene compds. useful in theatment and prophylaxis
        of different diseases)
ΤТ
     Tau proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (phosphorylation inhibitors, codrugs; preparation of nitrosated
        derivs. of dihydroxybenzene compds. useful in treatment and
        prophylaxis of different diseases)
     Analgesics
     Angiogenesis inhibitors
     Anti-inflammatory agents
     Antiarthritics
     Antiasthmatics
     Anticoagulants
     Antifibrotic agents
     Antihypertensives
     Antitumor agents
     Antiulcer agents
     Combination chemotherapy
     Cytotoxic agents
       Drugs
     Fibroblast
     Heart rate
     Hypolipemic agents
       Pharmaceutical carriers
       Pharmaceutical excipients
     Phosphorylation
       Prodrugs
     Prophylaxis
     Signal transduction
     Vasodilators
        (preparation of nitrosated derivs. of dihydroxybenzene compds. useful in
        treatment and prophylaxis of different diseases)
ΙT
     Skin, disease
        (rosacea, treatment of; preparation of nitrosated derivs. of
        dihydroxybenzene compds. useful in treatment and prophylaxis
        of different diseases)
     Keratosis
ΤТ
        (seborrheic, tweatment of; preparation of nitrosated derivs. of
        dihydroxybenzene compds. useful in treatment and prophylaxis
        of different diseases)
     Arthritis
ΤТ
     Asthma
     Atherosclerosis
     Crohn disease
     Dermatitis
     Eye, disease
     Fibrosis
     Glomerulonephritis
     Hemangioma
     Hyperlipidemia
     Hypertension
     Inflammation
     Neuroglia, neoplasm
     Pigmentation disorders
       Psoriasis
     Thrombosis
     Ulcerative colitis
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Serial#: 10/588,166 (treatment of; preparation of nitrosated derivs. of dihydroxybenzene compds. useful in treatment and prophylaxis of different diseases) ΙT 69-72-7, Salicylic acid, biological studies 1406-16-2D, Vitamin D, analogs RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (codrugs; preparation of nitrosated derivs. of dihydroxybenzene compds. useful in treatment and prophylaxis of different diseases) 1061696-45-4P RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); TAU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (drug candidate and intermediate; preparation of nitrosated derivs. of dihydroxybenzene compds. useful in treatment and prophylaxis of different diseases) 1061696-51-2P 1061696-54-5P 1061696-48-7P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (drug candidate; preparation of nitrosated derivs. of dihydroxybenzene compds. useful in treatment and prophylaxis of different diseases) 9001-08-5 ΙT RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor, codrugs; preparation of nitrosated derivs. of dihydroxybenzene compds. useful in treatment and prophylaxis of different diseases) 9036-21-9, Cyclic nucleotide phosphodiesterase 9068-52-4, CGMP TΤ phosphodiesterase RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors, codrugs; preparation of nitrosated derivs. of dihydroxybenzene compds. useful in treatment and prophylaxis of different diseases) 96627-32-6P 1061696-58-9P 1061696-60-3P 1061696-62-5P ΙT RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate; preparation of nitrosated derivs. of dihydroxybenzene compds. useful in treatment and prophylaxis of different diseases) 7665-99-8, CGMP 10102-43-9, Nitric oxide, biological studies ΤТ RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of nitrosated derivs. of dihydroxybenzene compds. useful in treatment and prophylaxis of different diseases) ΙT 100-02-7, 4-Nitrophenol, reactions 2067-33-6, 5-Bromovaleric acid 20123-80-2, Calcium dobesilate 21799-87-1 RL: RCT (Reactant); RACT (Reactant or reagent) (starting material; preparation of nitrosated derivs. of dihydroxybenzene compds. useful in treatment and prophylaxis of different diseases) 20123-80-2, Calcium dobesilate 21799-87-1 ΤT RL: RCT (Reactant); RACT (Reactant or reagent) (starting material; preparation of nitrosated derivs. of dihydroxybenzene

compds. useful in treatment and prophylaxis of different

Benzenesulfonic acid, 2,5-dihydroxy-, calcium salt (2:1) (CA INDEX NAME)

RN

CN

diseases)
20123-80-2 HCAPLUS

●1/2 Ca

RN 21799-87-1 HCAPLUS

CN Benzenesulfonic acid, 2,5-dihydroxy-, potassium salt (1:1) (CA INDEX NAME)



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L63 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2008:223400 HCAPLUS Full-text

DOCUMENT NUMBER: 148:276783

TITLE: 2,5-Dihydroxybenzene for the treatment of

psoriasis

INVENTOR(S): Cuevas Sanchez, Pedro; Gimenez Gallego, Guillermo;

Saenz de Tejada Gorman, Inigo; Angulo Frutos, Javier;

Valverde Lopez, Serafin; Romero Garrido, Antonio;

Lozano Puerto, Rosa Maria

PATENT ASSIGNEE(S): Action Medicines, S.L., Spain

SOURCE: PCT Int. Appl., 66pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE		
	A1 2008022	1 WO 2007-EP58443	20070815		
W: AE, AG, AL,	AM, AT, AU, AZ	, BA, BB, BG, BH, BR, BW,	BY, BZ, CA,		
CH, CN, CO,	CR, CU, CZ, DE	, DK, DM, DO, DZ, EC, EE,	EG, ES, FI,		
GB, GD, GE,	GH, GM, GT, HN	, HR, HU, ID, IL, IN, IS,	JP, KE, KG,		
KM, KN, KP,	KR, KZ, LA, LC	, LK, LR, LS, LT, LU, LY,	MA, MD, ME,		
MG, MK, MN,	MW, MX, MY, MZ	, NA, NG, NI, NO, NZ, OM,	PG, PH, PL,		
PT, RO, RS,	RU, SC, SD, SE	, SG, SK, SL, SM, SV, SY,	TJ, TM, TN,		
TR, TT, TZ,	UA, UG, US, UZ	, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG,	CH, CY, CZ, DE	, DK, EE, ES, FI, FR, GB,	GR, HU, IE,		
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BJ, CF, CG,	CI, CM, GA, GN	, GQ, GW, ML, MR, NE, SN,	TD, TG, BW,		

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Serial#: 10/588,166
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
     ES 2315118
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    US 20080125486
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                        A1 20090513 EP 2007-788429
                                                                  20070815
        R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR,
             AL, BA, HR, MK, RS
    MX 2009001660
                        A
                               20090424
                                         MX 2009-1660
                                                                  20090213
PRIORITY APPLN. INFO.:
                                           ES 2006-2218
                                                               A 20060816
                                           ES 2007-1856
                                                               A 20070702
                                           WO 2007-EP58443
                                                             W 20070815
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S):
                        MARPAT 148:276783
      The invention relates to the use of a 2,5-dihydroxybenzene derivative or a
pharmaceutically acceptable salt or solvate, isomer or prodrug thereof in preparing a
medicinal product for the treatment and/or prophylaxis of psoriasis. IPCI A61K0031-185
[I,A]; A61K0031-192 [I,A]; A61K0031-21 [I,A]; A61K0031-216
     [I,A]; A61K0031-255 [I,A]; A61P0017-06 [I,A]; A61P0017-00 [I,C*];
     A61K0031-60 [I,A]; A61K0045-06 [I,A]; A61K0045-00 [I,C*]
IPCR A61K0031-185 [I,C]; A61K0031-185 [I,A]; A61K0031-192 [I,A]; A61K0031-21
     [I,C]; A61K0031-21 [I,A]; A61K0031-216 [I,A]; A61K0031-255 [I,A];
     A61K0031-60 [I,C]; A61K0031-60 [I,A]; A61K0045-00 [I,C]; A61K0045-06
     [I,A]; A61P0017-00 [I,C]; A61P0017-06 [I,A]
CC
     1-12 (Pharmacology)
ST
    hydroxybenzene deriv psoriasis therapy
ΙT
     Epidermal growth factor receptors
     Fibroblast growth factor receptors
     Hepatocyte growth factor
     Hepatocyte growth factor receptors
     Vascular endothelial growth factor receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (antagonists; hydroxybenzene derivs. for treatment of
        psoriasis)
     Therapy
ΙT
        (coadjuvant; hydroxybenzene derivs. for treatment of
        psoriasis)
     Angiogenesis inhibitors
     Anti-inflammatory agents
     Antimicrobial agents
     Antioxidants
     Antitumor agents
     Apoptosis
     Buccal drug delivery systems
     Endothelin receptor antagonists
     Fibrosis
    Human
     Immunomodulators
     Lung, neoplasm
     Neuroglia, neoplasm
     Oral drug delivery systems
     Otic drug delivery systems
     Parenteral drug delivery systems
     Photodynamic therapy
      Phototherapy
       Prodrugs
     Prophylaxis
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Serial#: 10/588,166 Prostate gland, neoplasm Psoriasis Rectal drug delivery systems Topical drug delivery systems Transdermal drug delivery systems (hydroxybenzene derivs. for treatment of psoriasis) Corticosteroids, biological studies ΙT Retinoids Steroids, biological studies RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hydroxybenzene derivs. for treatment of psoriasis) ΤТ Fibroblast (mitogenesis; hydroxybenzene derivs. for treatment of psoriasis) 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor ΙT 127464-60-2, Vascular endothelial growth factor RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; hydroxybenzene derivs. for treatment of psoriasis) ΙT 106096-92-8, FGF-1 RL: BSU (Biological study, unclassified); BIOL (Biological study) (hydroxybenzene derivs. for treatment of psoriasis) 59-05-2, Methotrexate 69-72-7, Salicylic acid, biological studies ΤТ 88-46-0, 2,5-Dihydroxybenzenesulfonic acid 110-17-8D, 2-Butenedioic acid (2E)-, derivs. 123-31-9D, 1,4-Dihydroxybenzene, derivs. 490-79-9, Gentisic acid 636-01-1, 2,5-Dihydroxycinnamic acid 1406-16-2D, Vitamin D, analogs 21799-87-1, Potassium 2,5-Dihydroxybenzenesulfonate 21799-87-10, ester derivs. 51579-69-2 57775-26-5 59687-22-8 59865-13-3, Cyclosporin 60630-38-8 79122-68-2 159252-66-1 159252-66-1D, ester derivs. 170277-31-3, Infliximab 185243-69-0, Etanercept 214745-43-4, Efalizumab 222535-22-0, Alefacept 331731-18-1, Adalimumab 748106-93-6 1007839-71-5 1007839-72-6D, ester derivs. 1007839-87-31007839 - 89 - 5 1007839 - 91 - 9 1007839 - 93 - 1 1007839 - 94 - 2 1007839 - 96 - 4 $1007840 - 16 - 5 \qquad 1007840 - 17 - 6 \qquad 1007840 - 18 - 7 \qquad 1007840 - 19 - 8 \qquad 1007840 - 20 - 1$ $1007840 - 21 - 2 \qquad 1007840 - 22 - 3 \qquad 1007840 - 23 - 4 \qquad 1007840 - 24 - 5 \qquad 1007849 - 27 - 5$ RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hydroxybenzene derivs. for treatment of psoriasis) ΤТ 80449-02-1, Protein tyrosine kinase 141436-78-4, Protein kinase C RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; hydroxybenzene derivs. for treatment of psoriasis) ΙT 88-46-0, 2,5-Dihydroxybenzenesulfonic acid 21799-87-1, Potassium 2,5-Dihydroxybenzenesulfonate 21799-87-10, ester derivs. RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hydroxybenzene derivs. for treatment of psoriasis) RN 88-46-0 HCAPLUS Benzenesulfonic acid, 2,5-dihydroxy- (CA INDEX NAME) CN

RN 21799-87-1 HCAPLUS

CN Benzenesulfonic acid, 2,5-dihydroxy-, potassium salt (1:1) (CA INDEX

NAME)

● K

RN 21799-87-1 HCAPLUS

CN Benzenesulfonic acid, 2,5-dihydroxy-, potassium salt (1:1) (CA INDEX

NAME)

● K

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2007:705929 HCAPLUS Full-text

DOCUMENT NUMBER: 147:87646

TITLE: 2,5-Dihydroxybenzene sulfonate compounds for

treatment of cancer, rosacea, and

psoriasis

INVENTOR(S): Cuevas Sanchez, Pedro; Romero Garrido, Antonio;

Gimenez Gallego, Guillermo; Valverde Lopez, Serafin;

Lozano Puerto, Rosa Maria

PATENT ASSIGNEE(S): Action Medicines, S.L., Spain

SOURCE: U.S. Pat. Appl. Publ., 33pp., Cont.-in-part of U.S.

Ser. No. 588,166.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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Serial#: 10/588,166
     US 20070149618
                        A1 20070628 US 2006-506469
                                                                   20060816
     ES 2238924
                        A1
                               20050901 ES 2004-371
                                                                   20040217
     ES 2238924
                         В1
                               20061201
                        A1
                                         WO 2005-ES70017
     WO 2005077352
                                20050825
                                                                 20050216
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     US 20080125485
                         A1
                               20080529
                                            US 2007-839508
                                                                   20070815
                                           US 2008-257854
     US 20090111779
                         Α1
                                20090430
                                                                  20081024
                                                               A 20040217
PRIORITY APPLN. INFO.:
                                            ES 2004-371
                                            WO 2005-ES70017 W 20050216
US 2006-588166 A2 20060802
                                            ES 2006-2219
                                                              A 20060816
                                            US 2006-506469
                                                              A2 20060816
                                            ES 2007-1857
                                                              A 20070702
                                                              A2 20080807
                                            US 2008-588166
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB
     The invention describes compns. and methods of use for 2,5-dihydroxybenzene sulfonic
     acid compds. and pharmaceutically acceptable salts thereof. The invention provides
     methods for (a) treating skin cancer; (b) treating cancer of the organs; (c)
     treating leukemia; (d) improving the efficacy of chemotherapy, radiation therapy
     and/or cancer immunotherapy; (e) treating rosacea; and (f) treating psoriasis by
     administration of a composition comprising at least one 2,5-dihydroxybenzene
     sulfonic acid compound or a pharmaceutically acceptable salt thereof, and,
     optionally at least one therapeutic agent. Also disclosed are compns. comprising
     administration of at least one 2,5-dihydroxybenzene sulfonic acid compound, or a
     pharmaceutically acceptable salt thereof, and, at least one therapeutic agent. In
     the invention the 2,5-dihydroxybenzene sulfonic acid compds. or pharmaceutically
     acceptable salts thereof are 2,5-dihydroxybenzene sulfonic acid, calcium 2,5-
     dihydroxybenzenesulfonate, potassium 2,5-dihydroxybenzenesulfonate, magnesium 2,5-
     dihydroxybenzenesulfonate and diethylamine 2,5-dihydroxybenzenesulfonate.
     Administration of 2,5-dihydroxybenzene sulfonate combined with irinotecan reduced
     the tumor progression of gliomas in rats to a greater degree than tweatment of
     either agent alone.
INCL 514553000; 514171000; 514559000; 514167000; 514159000
IPCI A61K0031-185 [I,A]; A61K0031-60 [I,A]; A61K0031-59 [I,A]; A61K0031-56
IPCR A61K0031-185 [I,C]; A61K0031-185 [I,A]; A61K0031-56 [I,C]; A61K0031-56
     [I,A]; A61K0031-59 [I,C]; A61K0031-59 [I,A]; A61K0031-60 [I,C];
     A61K0031-60 [I,A]
    514/553.000; 514/159.000; 514/167.000; 514/171.000; 514/559.000
NCL
CC
     1-6 (Pharmacology)
ST
     dihydroxybenzene sulfonate cancer rosacea psoriasis
     therapy; glioma irinotecan dihydroxybenzene sulfonate antitumor
     combination
ΤТ
     Anti-inflammatory agents
     Antimicrobial agents
     Antioxidants
     Buccal drug delivery systems
     Chemosensitizers, pharmaceutical
       Chemotherapy
     Combination chemotherapy
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Cytotoxic agents

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Serial#: 10/588,166
     Dermatological agents
     Immunomodulators
     Inhalation drug delivery systems
     Leukemia
     Melanoma
     NMDA receptor antagonists
     Neuroglia, neoplasm
     Oral drug delivery systems
     Parenteral drug delivery systems
      Pharmaceutical carriers
      Pharmaceutical creams
     Proliferation inhibition
       Psoriasis
     Rectal drug delivery systems
     Skin, neoplasm
     Topical drug delivery systems
        (2,5-dihydroxybenzene sulfonate compds. for treatment of
        cancer, rosacea and psoriasis)
ΙT
     Retinoids
     Steroids
     RL: PAC (Pharmacological activity); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (2,5-dihydroxybenzene sulfonate compds. for treatment of
        cancer, rosacea and psoriasis)
ΙT
     Petrolatum
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (2,5-dihydroxybenzene sulfonate compds. for treatment of
        cancer, rosacea and psoriasis)
ΙT
     Carcinoma
     Skin, neoplasm
        (Bowen's disease, verrucae; 2,5-dihydroxybenzene sulfonate compds. for
        treatment of cancer, rosacea and psoriasis)
ΤТ
     Keratosis
        (actinic; 2,5-dihydroxybenzene sulfonate compds. for treatment
        of cancer, rosacea and psoriasis)
     Apoptosis
ΙT
        (basal cell carcinoma cells; 2,5-dihydroxybenzenesulfonate-induced;
        2,5-dihydroxybenzene sulfonate compds. for treatment of
        cancer, rosacea and psoriasis)
     Skin, neoplasm
ΤT
        (basal cell carcinoma; 2,5-dihydroxybenzene sulfonate compds. for
        treatment of cancer, rosacea and psoriasis)
ΙT
     Carcinoma
        (basal cell; 2,5-dihydroxybenzene sulfonate compds. for
        treatment of cancer, rosacea and psoriasis)
ΙT
     Carcinoma
        (cutaneous squamous cell; 2,5-dihydroxybenzene sulfonate compds. for
        treatment of cancer, rosacea and psoriasis)
ΙT
     Antitumor agents
       Immunotherapy
       Radiotherapy
        (efficacy; agents improving; 2,5-dihydroxybenzene sulfonate compds. for
        treatment of cancer, rosacea and psoriasis)
ΤТ
     Skin, neoplasm
        (keratoacanthoma; 2,5-dihydroxybenzene sulfonate compds. for
        treatment of cancer, rosacea and psoriasis)
ΙT
        (orangiosarcoma; 2,5-dihydroxybenzene sulfonate compds. for
        treatment of cancer, rosacea and psoriasis)
ΙT
     Drug interactions
        (pharmacodynamic, potentiation; 2,5-dihydroxybenzene
```

Serial#: 10/588,166 sulfonate compds. for treatment of cancer, rosacea and psoriasis) ΙT Skin, disease (rosacea; 2,5-dihydroxybenzene sulfonate compds. for treatment of cancer, rosacea and psoriasis) Neoplasm ΙT (solid; 2,5-dihydroxybenzene sulfonate compds. for treatment of cancer, rosacea and psoriasis) ΙT Skin, neoplasm (squamous cell carcinoma; 2,5-dihydroxybenzene sulfonate compds. for treatment of cancer, rosacea and psoriasis) ΙT Paraffin waxes RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (white soft; 2,5-dihydroxybenzene sulfonate compds. for treatment of cancer, rosacea and psoriasis) 51-21-8, 5-Fluorouracil 57-22-7, Vincristine 69-72-7, Salicylic acid, ΙT biological studies 88-46-0, 2,5-Dihydroxybenzenesulfonic acid 1406-16-2D, Vitamin D, analog 2624-44-4, Diethylamine 2,5-dihydroxybenzenesulfonate 15663-27-1, Cisplatin 20123-80-2 , Calcium 2,5-dihydroxybenzenesulfonate 21799-87-1, Potassium 2,5-dihydroxybenzenesulfonate 33069-62-4, Paclitaxel 68864-98-2, 2,5-Dihydroxybenzenesulfonate 97225-83-7, Magnesium 2,5-dihydroxybenzenesulfonate 97682-44-5, Irinotecan 100286-90-6, Campto RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (2,5-dihydroxybenzene sulfonate compds. for treatment of cancer, rosacea and psoriasis) ΙT 112-92-5, Stearic alcohol 7732-18-5, Water, biological studies 36653-82-4, Cetylic alcohol 942134-54-5, Sorbinate deato RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (2,5-dihydroxybenzene sulfonate compds. for treatment of cancer, rosacea and psoriasis) 116243-73-3, Endothelin ΤT RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonist; 2,5-dihydroxybenzene sulfonate compds. for treatment of cancer, rosacea and psoriasis) 88-46-0, 2,5-Dihydroxybenzenesulfonic acid 2624-44-4 ΙT , Diethylamine 2,5-dihydroxybenzenesulfonate 20123-80-2, Calcium 2,5-dihydroxybenzenesulfonate 21799-87-1, Potassium 2,5-dihydroxybenzenesulfonate 68864-98-2, 2,5-Dihydroxybenzenesulfonate RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (2,5-dihydroxybenzene sulfonate compds. for treatment of cancer, rosacea and psoriasis)

Benzenesulfonic acid, 2,5-dihydroxy- (CA INDEX NAME)

RN CN 88-46-0 HCAPLUS

RN

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Serial#: 10/588,166
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Benzenesulfonic acid, 2,5-dihydroxy-, compd. with N-ethylethanamine (1:1) (CA INDEX NAME) CM 1 CRN 109-89-7 CMF C4 H11 N CM2 CRN 88-46-0 CMF C6 H6 O5 S 20123-80-2 HCAPLUS RN Benzenesulfonic acid, 2,5-dihydroxy-, calcium salt (2:1) (CA INDEX NAME) CN ОН SO3H $\bigcirc 1/2$ Ca 21799-87-1 HCAPLUS RN Benzenesulfonic acid, 2,5-dihydroxy-, potassium salt (1:1) (CA INDEX CN NAME)

K

CN

RN 68864-98-2 HCAPLUS

Benzenesulfonic acid, 2,5-dihydroxy-, ion(1-) (CA INDEX NAME)

L63 ANSWER 7 OF 8 WPIX COPYRIGHT 2010 THOMSON REUTERS on STN

ACCESSION NUMBER: 2008-N22597 [200877] WPIX

TITLE: New cinnamic amide derivative useful for treating

diseases responsive to modulation of potassium channel,

e.g., respiratory diseases, convulsion, erectile dysfunction, gastrointestinal dysfunction, ischemia,

schizophrenia and sleep disorder

DERWENT CLASS: B0

INVENTOR: CHRISTOPHERSEN P; DEMNITZ J; GRUNNET M; JENSEN T; JENSEN

T D; JONES D; JONES D S; MADSEN L; MADSEN L S; NARDI A;

NIELSEN E; NIELSEN E O; STROBAK D; STROBAEK D

PATENT ASSIGNEE: (NURO-C) NEUROSEARCH AS

COUNTRY COUNT: 121

PATENT INFO ABBR.:

PATENT NO	KIND DATE	KIND DA	WEEK	LA	PG	MAIN IPC
WO 2008074755	A2 20080626		,		45[1]	
WO 2008074755	A3 20081002		,			
EP 2121569	A2 20091125		/	EN		
US 20100087496		_	,	EN	4.77	
JP 2010513387	W 20100430	w 201	(201029)	JA	4 /	

APPLICATION DETAILS:

PA:	IENT NO	KIND	API	PLICATION	DATE
WO	2008074755	A2	WO	2007-EP64015	5 20071217
US	20100087496	Al Provisional	US	2006-870781E	20061219
EP	2121569 A2		EP	2007-857649	20071217

EP 2121569 A2 PCT Application WO 2007-EP64015 20071217
US 20100087496 A1 PCT Application WO 2007-EP64015 20071217
US 20100087496 A1 US 2009-519683 20090724
JP 2010513387 W PCT Application WO 2007-EP64015 20071217
JP 2010513387 W JP 2009-542019 20071217

FILING DETAILS:

	PATENT NO			KIND			PATENT NO		
	EP 2121569 JP 2010513387		A2 W	Based on Based on			2008074755 2008074755	 А А	
PRIOR:	ITY	APPLN.	INFO:	DK 2	007-481 006-1657 006-870781P	2	2006	70328 51218 51219	
		000000							

AB WO 2008074755 A2 UPAB: 20091126

NOVELTY - A cinnamic amide derivative (I), is new.

DETAILED DESCRIPTION - A cinnamic amide derivative of formula (I), or its enantiomer, mixture of its enantiomers, or salt, is new.

R1=nitro, amino, hydroxy, carboxy, sulfonic acid, sulfonic acid alkyl ester, sulfamoyl, acetamido, methyl-sulfonyl-amino, phenyl-sulfonyl-amino, N-methyl-sulfonyl-carboxamide (methyl-sulfonyl-amino-carbonyl), N-phenyl-sulfonyl-carboxamide (phenyl-sulfonyl-amino-carbonyl), trifluoromethyl-sulfonyl-amino, trifluoromethyl-acetyl-amino, 2,2,2-trifluoro-1-hydroxy-1-trifluoromethyl- ethyl, tetrazolyl, tetrazolyl-methoxy, 5-oxo-4,5-dihydro-(1,2,4)oxadiazol-3-yl or N-cyano-carboxamide;

R2 and R3=phenyl (optionally substituted with halo and/or trifluoromethyl), H, halo, trifluoromethyl, or hydroxy;

R4 and R5=H, halo, trifluoromethyl, nitro and/or phenyl;or

R4 and R5 together with the aromatic ring to which they are attached=benzo-fused carbocyclic aromatic ring;

R' and R'a=H; or

R' and R'a together with the carbon atoms of the aromatic ring to which they are attached=bicyclic carbocyclic or heterocyclic ring selected from 2H-chromenyl (optionally substituted with oxo to form a 2-oxo-2H-chromenyl derivative), or indolyl.

INDEPENDENT CLAIMS are included for the following:

- (1) use of a combination of a cinnamic amide derivative (I); and a phosphodiesterase inhibitor; or an agent that potentiates endothelium-derived hyperpolarizing factor-mediated responses; or their salts, for the manufacture of a medicament for the treatment or alleviation of sexual dysfunction; and
- (2) a kit of parts comprising at least two separate unit dosage forms cinnamic amide derivative (I); and a phosphodiesterase inhibitor; or an agent that potentiates endothelium-derived hyperpolarizing factor-mediated responses; and optionally instructions for the simultaneous, sequential or separate administration of the cinnamic amide derivative (I), and the phosphodiesterase inhibitor, or the agent, to a patient.

ACTIVITY - Respiratory-Gen.; Anticonvulsant; Vasotropic; Cardiant; CNS-Gen.; Muscular-Gen.; Nephrotropic; Uropathic; Hepatotropic; Gastrointestinal-Gen.; Laxative; Antidiarrheic; Cerebroprotective; Vulnerary; Antianginal; Antiparkinsonian; Neuroleptic; Nootropic; Tranquilizer; Antidepressant; Antimanic; Neuroprotective; Analgesic; Gynecological; Hypnotic; Immunosuppressive; Antiarrhythmic; Cardiovascular-Gen.; Hypotensive; Relaxant; Antidiabetic; Tocolytic; Cytostatic; Antiinflammatory; Auditory; Antimigraine; Endocrine-gen.; Ophthalmological; Osteopathic; Angiogenesis-inhibitor; Antiarthritic; Antirheumatic; Antipsoriatic; Antianemic.

MECHANISM OF ACTION - Ion channel modulator e.g. calcium activated potassium (BK) channel modulator. (E)-N-(5-chloro-2-(1H-tetrazol-5-yl)- phenyl)-3-naphthalen-2-yl-acrylamide (I') was tested for BK channel opening activity using BK channels heterologously expressed in Xenopus laevis oocytes in terms of current. BK current

was activated by repeated step protocols. The compound (I') (1 mu M) was added. The compound (I') showed marked increased in current of 6-9 mu M at 80-134 seconds.

USE - In the manufacture of a pharmaceutical composition/medicament for treating respiratory disease, epilepsy, convulsions, seizures, absence seizures, vascular spasms, coronary artery spasms, motor neuron diseases, myokymia, renal disorders, polycystic kidney disease, bladder hyperexcitability, bladder spasms, urinogenital disorders, urinary incontinence, bladder outflow obstruction, erectile dysfunction, gastrointestinal dysfunction, gastrointestinal hypomotility disorders, gastrointestinal motility insufficiency, postoperative ileus, constipation, gastroesophageal reflux disorder, secretory diarrhea, ischemia, cerebral ischemia, ischemic heart disease, angina pectoris, coronary heart disease, ataxia, traumatic brain injury, stroke, Parkinson's disease, bipolar disorder, psychosis, schizophrenia, autism, anxiety, mood disorders, depression, manic depression, psychotic disorders, dementia, learning deficiencies, age related memory loss, memory and attention deficits, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), dysmenorrhea, narcolepsy, sleeping disorders, sleep apnea, Raynaud's disease, intermittent claudication, Sjogren's syndrome, xerostomia, arrhythmia, cardiovascular disorders, hypertension, myotonic dystrophy, myotonic muscle dystrophia, spasticity, xerostomia, diabetes Type II, hyperinsulinemia, premature labor, cancer, brain tumors, inflammatory bowel disease, irritable bowel syndrome, colitis, colitis Crohn', immune suppression, hearing loss, migraine, pain, neuropathic pain, inflammatory pain, trigeminal neuralgia, vision loss, rhinorrhoea, ocular hypertension (glaucoma), baldness, cardiac arrhythmia, atrial arrhythmia, ventricular arrhythmia, atrial fibrillation, ventricular fibrillation, tachyarrhythmia, atrial tachyarrhythmia, ventricular tachyarrhythmia, bradyarrhythmia, or any other abnormal rhythm, e.g. caused by myocardial ischemia, myocardial infarction, cardiac hypertrophy or cardiomyopathy disease/disorder/condition responsive to modulation of potassium channel in a mammal including a human, and for treating sexual dysfunction i.e. male dysfunction and female dysfunction (claimed); and also for treating diseases such as bone metabolic disease, disease that is responsive to inhibition of angiogenesis, an ophthalmic angiogenesis related diseases, rheumatoid arthritis, psoriasis and sickle-cell anemia, and pain.

ADVANTAGE - The compound are potent ion channel modulator and treats disease, disorder or condition responsive to modulation of potassium channels without any harmful side effects. The compounds show calcium activated potassium channel opening activity in sub-micromolar and micromolar range, i.e., from below 1-100 mu M.

AN.S DCR-89832

CN.P CALCIUM DOBESILATE

CN.S Calcium; 2,5-dihydroxy-benzenesulfonate

SDCN R20556

CM 1

Ca

CM 2

L63 ANSWER 8 OF 8 WPIX COPYRIGHT 2010 THOMSON REUTERS on STN ACCESSION NUMBER: 1996-020345 [199602] WPIX
DOC. NO. CPI: C1996-006976 [199602]
TITLE: Opiate antagonist and calcium salt in compsn. - for

treatment of endorphin-mediated pathologies B05; C03

DERWENT CLASS:

INVENTOR: CIORCI R L; MINOIA P; SCIORSCI R L

(CIOR-I) CIORCI R L; (MINO-I) MINOIA P; (RAPH-I) RAPHAEL PATENT ASSIGNEE:

L G; (SCIO-I) SCIORSCI R; (SCIO-I) SCIORSCI R L; (EXCE-N)

EXCELSIOR LIFE SCI IRELAND LTD

COUNTRY COUNT: 64

PATENT INFO ABBR.:

PATENT NO	KIN	D DATE	WEEK	LA	PG	MAIN IPC
WO 9531985	A2	19951130	(199602)*	EN	19[0]	
AU 9526149	А	19951218	(199611)	ΕN		
WO 9531985	А3	19960104	(199622)	ΕN		
EP 760661	A1	19970312	(199715)	ΕN	[0]	
IT 1269826	В	19970415	(199744)	ΙT		
JP 10500423	W	19980113	(199812)	JA	19[0]	
KR 97703148	A	19970703	(199829)	KO		
US 5811451	А	19980922	(199845)	ΕN		
HU 77920	T	19981028	(199850)	HU		
EP 760661	В1	19981230	(199905)	ΕN		
DE 69507029	E	19990211	(199912)	DE		
ES 2128735	Т3	19990516	(199926)	ES		
AU 708778	В	19990812	(199944)	ΕN		
CN 1151116	A	19970604	(200131)	ZH		
CN 1083264	С	20020424	(200519)	ZH		
JP 2007210995	Α	20070823	(200757)	JA	11	
CA 2190943	С	20100622	(201045)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DA	ATE
WO 9531985 A2 IT 1269826 B AU 9526149 A		WO 1995-EP1931 19 IT 1994-MI1048 19 AU 1995-26149 199	9940524
AU 708778 B CN 1151116 A CN 1083264 C		AU 1995-26149 199 CN 1995-193758 19 CN 1995-193758 19	9950522
DE 69507029 E EP 760661 A1		DE 1995-69507029 EP 1995-920851 19	19950522 9950522
EP 760661 B1 DE 69507029 E ES 2128735 T3		EP 1995-920851 19 EP 1995-920851 19 EP 1995-920851 19	9950522
JP 10500423 W JP 2007210995 .	A Div Ex	JP 1995-530058 19 JP 1995-530058 19	9950522 9950522
WO 9531985 A3 EP 760661 A1 JP 10500423 W		WO 1995-EP1931 19 WO 1995-EP1931 19 WO 1995-EP1931 19	9950522
KR 97703148 A US 5811451 A		WO 1995-EP1931 19 WO 1995-EP1931 19	9950522 9950522
HU 77920 T EP 760661 B1 DE 69507029 E		WO 1995-EP1931 19 WO 1995-EP1931 19 WO 1995-EP1931 19	9950522

HU 77920 T

KR 97703148 A

KR 1996-706602 19961121

US 5811451 A

US 1996-737902 19961121

JP 2007210995 A

JP 2006-303392 20061108

CA 2190943 C

FILING DETAILS:

PATENT NO	KIND		PATENT NO			
AU 708778	В	Previous Publ	AU 9526149	A		
DE 69507029	E	Based on	EP 760661	Α		
ES 2128735	Т3	Based on	EP 760661	Α		
AU 9526149	А	Based on	WO 9531985	Α		
EP 760661	A1	Based on	WO 9531985	Α		
JP 10500423	W	Based on	WO 9531985	Α		
KR 97703148	A	Based on	WO 9531985	Α		
US 5811451	Α	Based on	WO 9531985	Α		
HU 77920	T	Based on	WO 9531985	Α		
EP 760661	B1	Based on	WO 9531985	Α		
DE 69507029	E	Based on	WO 9531985	Α		
AU 708778	В	Based on	WO 9531985	Α		
CA 2190943	С	Based on	WO 9531985	Α		

PRIORITY APPLN. INFO: IT 1994-MI1048 19940524

WO 1995031985 A2 UPAB: 20050702

A pharmaceutical compsn. essentially comprises an opiate antagonist and a calcium salt.

USE - The compsn. is for the treatment of endorphin-mediated pathologies, including diseases of the CNS e.g. paraplegia, nervous conducibility disturbances, Alzheimer's disease, cerebral ischaemia and multiple sclerosis; gastrointestinal diseases such as ulcers and irritable bowel syndrome; cardiovascular diseases such as infarct and septic shock; dermatological diseases such as vitiligo, psoriasis, alopecia, dermatitis, traumatic injuries and burns; endocrinological and genitourinary diseases such as LUF syndrome, ovaric micropolyaptosis, impotence, hyperprolattinemia, hypophysary dwarfism, interstitial cystitis and primary amenhorrea; and also inflammatory conditions; infectious diseases, diseases of the muscle-skeletal system such as osteoporosis, arthritis, ostitis, periostitis, myopathies and autoimmune diseases; also, in veterinary medicine, the treatment of puerperal shock in bovines, viral diseases in dogs and cats, MMA syndrome, Mulberry's heart disease, ruminal meteorism, Hoflund syndrome and osteo-articular traumas, and also for controlling reproductive activity in mammals, fish and birds, for inducing the lysis of the corpus luteum, to improve athletic performance in horses and dogs; and in contraception.

AN.S DCR-89832

CN.P CALCIUM DOBESILATE

CN.S Calcium; 2,5-dihydroxy-benzenesulfonate

SDCN R20556

CM 1

Ca

CM 2

SEARCH HISTORY

```
FILE 'HCAPLUS' ENTERED AT 16:42:29 ON 22 JUL 2010
              E US2008-588166/APPS
L1
             3 SEA SPE=ON ABB=ON PLU=ON US2008-588166/APPS
               D SCAN
    FILE 'REGISTRY' ENTERED AT 16:43:18 ON 22 JUL 2010
               STRUCTURE UPLOADED
L2
               D
L3
            23 SEA SSS SAM L2
L4
           575 SEA SSS FUL L2
               STRUCTURE UPLOADED
L5
            23 SEA SUB=L4 SSS SAM L5
L7
           569 SEA SUB=L4 SSS FUL L5
    FILE 'HCAPLUS' ENTERED AT 16:47:38 ON 22 JUL 2010
          1313 SEA SPE=ON ABB=ON PLU=ON L7
L8
L9
         21558 SEA SPE=ON ABB=ON PLU=ON PSORIASIS+PFT/CT OR (?PSORIASIS?
               OR ?PUSTULOSIS?)/BI
             6 SEA SPE=ON ABB=ON PLU=ON L8 AND L9
           553 SEA SPE=ON ABB=ON PLU=ON L8 AND ((BAC OR DMA OR PAC OR PKT
L11
               OR THU)/RL OR (?THERA? OR ?PHARM? OR ?DRUG? OR ?TREAT?)/BI)
             6 SEA SPE=ON ABB=ON PLU=ON L11 AND L9
L12
             6 SEA SPE=ON ABB=ON PLU=ON L10 OR L12
L13
    FILE 'REGISTRY' ENTERED AT 16:54:16 ON 22 JUL 2010
             1 SEA SPE=ON ABB=ON PLU=ON "2,5-DIHYDROXYBENZENESULFONIC
L14
               ACID"/CN
    FILE 'HCAPLUS' ENTERED AT 16:58:43 ON 22 JUL 2010
           181 SEA SPE=ON ABB=ON PLU=ON L14
L15
            68 SEA SPE=ON ABB=ON PLU=ON L15 AND ((BAC OR DMA OR PAC OR PKT
L16
               OR THU)/RL OR (?THERA? OR ?PHARM? OR ?DRUG? OR ?TREAT?)/BI)
L17
             5 SEA SPE=ON ABB=ON PLU=ON L16 AND L9
             6 SEA SPE=ON ABB=ON PLU=ON L13 OR L17
L18
    FILE 'REGISTRY' ENTERED AT 16:59:51 ON 22 JUL 2010
               E "2,5-DIHYDROXYBENZENESULFONIC ACID"/CN
             4 SEA SPE=ON ABB=ON PLU=ON ("2,5-DIHYDROXYBENZENESULFONIC
L19
               ACID CALCIUM SALT"/CN OR "2,5-DIHYDROXYBENZENESULFONIC ACID
               DIETHYLAMINE SALT"/CN OR "2,5-DIHYDROXYBENZENESULFONIC ACID
               MONOSODIUM SALT"/CN OR "2,5-DIHYDROXYBENZENESULFONIC ACID
               MONOTOSYLATE MORPHOLINE SALT"/CN OR "2,5-DIHYDROXYBENZENESULFON
               IC ACID SODIUM SALT"/CN)
    FILE 'HCAPLUS' ENTERED AT 17:00:36 ON 22 JUL 2010
L20
           494 SEA SPE=ON ABB=ON PLU=ON L19
L21
           359 SEA SPE=ON ABB=ON PLU=ON L20 AND ((BAC OR DMA OR PAC OR PKT
               OR THU)/RL OR (?THERA? OR ?PHARM? OR ?DRUG? OR ?TREAT?)/BI)
L22
             4 SEA SPE=ON ABB=ON PLU=ON L21 AND L9
            6 SEA SPE=ON ABB=ON PLU=ON L22 OR L18
L23
L24
          2346 SEA SPE=ON ABB=ON PLU=ON SANCHEZ P?/AU
L25
          205 SEA SPE=ON ABB=ON PLU=ON GARRIDO A?/AU
           71 SEA SPE=ON ABB=ON PLU=ON GALLEGO G?/AU
L27
         2879 SEA SPE=ON ABB=ON PLU=ON LOPEZ S?/AU
            1 SEA SPE=ON ABB=ON PLU=ON PUERTO R?/AU
L28
             O SEA SPE=ON ABB=ON PLU=ON L23 AND ((L24 OR L25 OR L26 OR L27
L29
```

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Serial#: 10/588,166
               OR L28))
L30
             3 SEA SPE=ON ABB=ON PLU=ON L1 AND L23
L31
             O SEA SPE=ON ABB=ON PLU=ON L8 AND ((L24 OR L25 OR L26 OR L27
               OR L28))
L32
             O SEA SPE=ON ABB=ON PLU=ON L24 AND L25 AND L26 AND L27 AND
               L28
             5 SEA SPE=ON ABB=ON PLU=ON L24 AND ((L25 OR L26 OR L27 OR
L33
              L28))
L34
             O SEA SPE=ON ABB=ON PLU=ON L25 AND ((L26 OR L27 OR L28))
L35
             O SEA SPE=ON ABB=ON PLU=ON L26 AND ((L27 OR L28))
             O SEA SPE=ON ABB=ON PLU=ON L27 AND L28
L36
               D SCAN L33 TI
     FILE 'WPIX' ENTERED AT 17:06:19 ON 22 JUL 2010
             4 SEA SSS SAM L5
L37
L38
            31 SEA SSS FUL L5
            99 SEA SPE=ON ABB=ON PLU=ON L38/DCR
L39
             4 SEA SPE=ON ABB=ON PLU=ON L39 AND (?PSORIASIS? OR ?PUSTULOSIS
L40
               ?)
           113 SEA SPE=ON ABB=ON PLU=ON SANCHEZ P?/AU
L41
L42
           21 SEA SPE=ON ABB=ON PLU=ON GARRIDO A?/AU
L43
           13 SEA SPE=ON ABB=ON PLU=ON GALLEGO G?/AU
           142 SEA SPE=ON ABB=ON PLU=ON LOPEZ S?/AU
L44
             8 SEA SPE=ON ABB=ON PLU=ON PUERTO R?/AU
L45
             O SEA SPE=ON ABB=ON PLU=ON L40 AND ((L41 OR L42 OR L43 OR L44
L46
               OR L45))
             O SEA SPE=ON ABB=ON PLU=ON L41 AND L42 AND L43 AND L44 AND
L47
              L45
L48
             2 SEA SPE=ON ABB=ON PLU=ON L41 AND ((L42 OR L43 OR L44 OR
               L45))
             1 SEA SPE=ON ABB=ON PLU=ON L42 AND ((L43 OR L44 OR L45))
L49
             1 SEA SPE=ON ABB=ON PLU=ON L43 AND ((L44 OR L45))
L50
             O SEA SPE=ON ABB=ON PLU=ON L44 AND L45
L51
L52
             2 SEA SPE=ON ABB=ON PLU=ON (L48 OR L49 OR L50)
     FILE 'BEILSTEIN' ENTERED AT 17:11:11 ON 22 JUL 2010
             6 SEA SSS SAM L5
L53
L54
           137 SEA SSS FUL L5
L55
            17 SEA SPE=ON ABB=ON PLU=ON L54 AND BABSAN/FA
               SEL BABSAN L55
     FILE 'BABS' ENTERED AT 17:12:38 ON 22 JUL 2010
L56
            34 SEA SPE=ON ABB=ON PLU=ON (5779456/BABSAN OR 5795277/BABSAN
               OR 5824898/BABSAN OR 5514361/BABSAN OR 5640811/BABSAN OR
               5663724/BABSAN OR 5513340/BABSAN OR 5650706/BABSAN OR 5661677/B
               ABSAN OR 5664312/BABSAN OR 5683633/BABSAN OR 5716795/BABSAN OR
               5720015/BABSAN OR 5721112/BABSAN OR 5729262/BABSAN OR 5735774/B
               ABSAN OR 5742821/BABSAN OR 5795962/BABSAN OR 5821526/BABSAN OR
               5823978/BABSAN OR 5833257/BABSAN OR 5834887/BABSAN OR 5864226/B
               ABSAN OR 5883193/BABSAN OR 6272676/BABSAN OR 6307749/BABSAN OR
               6456010/BABSAN OR 6467490/BABSAN OR 6487461/BABSAN OR 6491941/B
               ABSAN OR 6536509/BABSAN OR 6574272/BABSAN OR 6575150/BABSAN OR
               6607291/BABSAN OR 6649109/BABSAN)
L57
             O SEA SPE=ON ABB=ON PLU=ON L56 AND (PSORIASIS? OR PUSTULOSIS?)
     FILE 'BEILSTEIN' ENTERED AT 17:16:22 ON 22 JUL 2010
L58
           120 SEA SPE=ON ABB=ON PLU=ON L54 NOT L55
L59
            67 SEA SPE=ON ABB=ON PLU=ON L58 AND (PRY<=2004 OR AY<=2004 OR
               PY <= 2004 OR PD <= 2004)
               D IDE
```

FILE 'REGISTRY' ENTERED AT 17:21:41 ON 22 JUL 2010

FILE 'HCAPLUS' ENTERED AT 17:21:44 ON 22 JUL 2010 D STAT QUE L33

FILE 'WPIX' ENTERED AT 17:21:54 ON 22 JUL 2010 D STAT QUE L52

FILE 'HCAPLUS, WPIX' ENTERED AT 17:22:10 ON 22 JUL 2010
L60 7 DUP REMOVE L33 L52 (0 DUPLICATES REMOVED)

ANSWERS '1-5' FROM FILE HCAPLUS

ANSWERS '6-7' FROM FILE WPIX

D L60 IBIB ABS HITIND HITSTR 1-5 D L60 IBIB AB HITSTR 6-7

FILE 'HCAPLUS' ENTERED AT 17:22:51 ON 22 JUL 2010
D STAT QUE L23

L61 6 SEA SPE=ON ABB=ON PLU=ON L23 NOT L33

FILE 'WPIX' ENTERED AT 17:23:02 ON 22 JUL 2010
D STAT QUE L40

L62 4 SEA SPE=ON ABB=ON PLU=ON L40 NOT L52

FILE 'HCAPLUS, WPIX' ENTERED AT 17:23:38 ON 22 JUL 2010 L63 8 DUP REMOVE L61 L62 (2 DUPLICATES REMOVED)

ANSWERS '1-6' FROM FILE HCAPLUS

ANSWERS '7-8' FROM FILE WPIX
D L63 IBIB ABS HITIND HITSTR 1-6
D L63 IBIB AB HITSTR 7-8

=>

ΩН

Uploading 10588166.str

0H

11

3
5
8

chain nodes :
7 8 9 10 11 12
ring nodes :
1 2 3 4 5 6
chain bonds :
1-12 4-11 6-7 7-8 7-9 7-10
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 1-12 2-3 3-4 4-5 4-5

1-2 1-6 1-12 2-3 3-4 4-5 4-11 5-6 6-7 7-8 7-9 7-10

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS

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Uploading LL5.str
```

chain nodes :
7 8 9 10 11 12
ring nodes :
1 2 3 4 5 6
chain bonds :
1-12 4-11 6-7 7-8 7-9 7-10
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-12 4-11 6-7
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-9 7-10

Match level:
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS